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Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder:

A Systematic Review Update

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Psychological and Pharmacological Treatments for Adults With Posttraumatic Stress Disorder: A Systematic Review Update

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The information in this report is intended to help health care decisionmakers—patients and clinicians, health system leaders, and policymakers, among others—make well-informed decisions and thereby improve the quality of health care services. This report is not intended to be a substitute for the application of clinical judgment. Anyone who makes decisions concerning the provision of clinical care should consider this report in the same way as any medical reference and in conjunction with all other pertinent information, i.e., in the context of available resources and circumstances presented by individual patients.

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Preface

The Agency for Healthcare Research and Quality (AHRQ), through its Evidence-based Practice Centers (EPCs), sponsors the development of evidence reports and technology assessments to assist public- and private-sector organizations in their efforts to improve the quality of health care in the United States.

The Patient-Centered Outcomes Research Institute (PCORI) was established to fund research that can help patients and those who care for them make better informed decisions about the health care choices they face every day. PCORI partnered with AHRQ to help fulfill PCORI's authorizing mandate to engage in evidence synthesis and make information from comparative effectiveness research more available to patients and providers. PCORI identifies topics for review based on broad stakeholder interest. After identifying specific topics, multistakeholder virtual workshops are held by PCORI to inform the individual research protocols.

The reports and assessments provide organizations, patients, clinicians, and caregivers with comprehensive, evidence-based information on common medical conditions and new health care technologies and strategies. They also identify research gaps in the selected scientific area, identify methodological and scientific weaknesses, suggest research needs, and move the field forward through an unbiased, evidence-based assessment of the available literature. The EPCs systematically review the relevant scientific literature on topics assigned to them by AHRQ and conduct additional analyses when appropriate prior to developing their reports and assessments.

To bring the broadest range of experts into the development of evidence reports and health technology assessments, AHRQ encourages the EPCs to form partnerships and enter into collaborations with other medical and research organizations. The EPCs work with these partner organizations to ensure that the evidence reports and technology assessments they produce will become building blocks for health care quality improvement projects throughout the Nation. The reports undergo peer review and public comment prior to their release as a final report.

AHRQ expects that the EPC evidence reports and technology assessments, when appropriate, will inform patients and caregivers, individual health plans, providers, and purchasers as well as the health care system as a whole by providing important information to help improve health care quality.

If you have comments on this evidence report, they may be sent by mail to the Task Order Officer: Aysegul Gozu, M.D., M.P.H., Agency for Healthcare Research and Quality, 5600 Fishers Lane, Rockville, MD 20857, or by email to epc@ahrq.hhs.gov.

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Evidence Summary

Introduction

This systematic review uses current methods to update a report published in 2013 that evaluated psychological and pharmacological treatments of adults with posttraumatic stress disorder (PTSD). This review focuses on updating the earlier work, expanding the range of treatments examined, addressing earlier uncertainties, identifying ways to improve care for PTSD patients, and reducing variation in existing treatment guidelines. Treatments examined are shown in Table A.The analytic framework that guides our review is shown in Figure A.

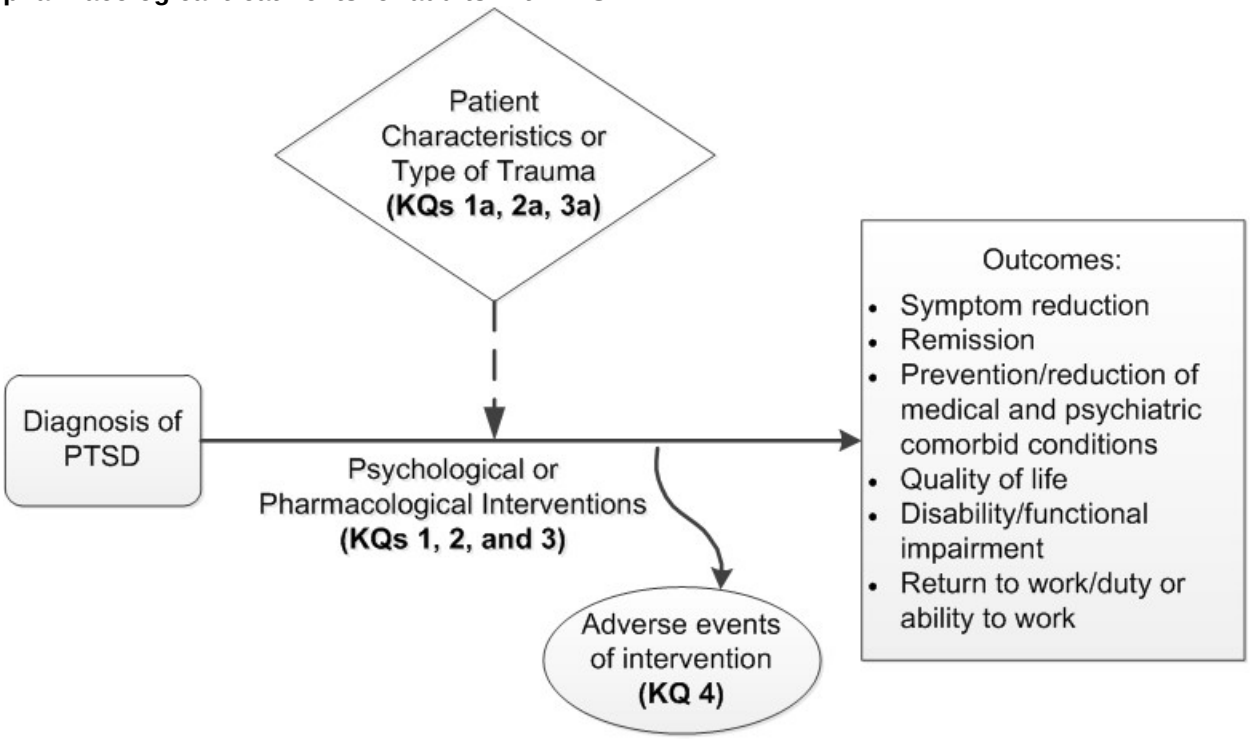
Table A. Psychological and pharmacological interventions used for treatment of patients with PTSD

Psychological Interventions	Pharmacological Interventions
Cognitive behavioral therapy • Cognitive processing therapy • Cognitive restructuring • Exposure-based therapies • Coping skills therapy • Various "mixed" therapies Eye movement desensitization and reprocessing Other psychological or behavioral therapies • Psychodynamic therapy • Interpersonal therapy • Hypnosis/hypnotherapy • Mindfulness-based stress reduction • Eclectic psychotherapy • Brainwave neurofeedback **Energy psychology**	Selective serotonin reuptake inhibitors: • Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline Selective serotonin and norepinephrine reuptake inhibitors: • Desvenlafaxine, venlafaxine, and duloxetine Tricyclic antidepressants: • Imipramine, amitriptyline, and desipramine Other second-generation antidepressants: • Bupropion, mirtazapine, nefazodone, and trazodone Alpha blockers: • Prazosin Second-generation (atypical) antipsychotics: • Olanzapine, risperidone, **ziprasidone, aripiprazole** and **quetiapine** Anticonvulsants (mood stabilizers): • Topiramate, tiagabine, lamotrigine, carbamazepine, and divalproex Benzodiazepines: • Alprazolam, diazepam, lorazepam, and clonazepam Other medications: **Naltrexone, cycloserine, and inositol**

PTSD = posttraumatic stress disorder. Bold: newly included treatment type examined in this updated review.

NOTE: The references for the Evidence Summary are included in the reference list that follows the appendixes.

Figure A. Analytic framework for the comparative effectiveness of psychological treatments and pharmacological treatments for adults with PTSD



KQ = Key Question; PTSD = posttraumatic stress disorder.

Results/Key Findings

- We used information from 207 published articles reporting on 193 studies to answer our Key Questions (KQs).
- KQ 1 (Psychological Treatment) Findings (Table B)
  - Two types of cognitive behavioral therapy (CBT) treatments had high strength of evidence (SOE) of benefit in reducing PTSD-related outcomes. These treatments included CBT-exposure and CBT-mixed treatments (CBT-mixed was a term we used to combine CBT treatments that had different types of CBT characteristics).
  - Other psychological treatments with moderate SOE of benefit included cognitive processing therapy (CPT), cognitive therapy (CT), eye movement desensitization and reprocessing (EMDR), and narrative exposure therapy (NET).
  - Moderate strength of evidence favored CBT-exposure over relaxation for reducing PTSD-related outcomes.
- KQ 2 (Pharmacological Treatment) Findings (Table C)
  - Moderate SOE of benefit in reduction in PTSD-related outcomes for fluoxetine, paroxetine, and venlafaxine as compared with placebo.

Table B. Summary of efficacy and strength of evidence of PTSD psychological treatments

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Cognitive processing therapy (CPT)	PTSD Symptoms[a]	5 (399)[1]	Reduced PTSD symptoms SMD -1.35 (95% CI, -1.77 to -0.94)	Moderate
	Loss of PTSD Diagnosis	4 (299)[1-4]	Greater loss of PTSD diagnosis RD 0.44 (95% CI, 0.26 to 0.62)	Moderate
	Depression Symptoms[b]	5 (399)[1-6]	Reduced depression symptoms SMD -1.09 (95% CI, -1.52 to -0.65)	Moderate
Cognitive therapy (CT)	PTSD Symptoms[a]	4 (283)[5, 7-9]	Reduced PTSD symptoms SMD of individual studies ranged from -2.0 to -0.3 All studies favored treatment (all studies p<0.05)	Moderate
	Loss of PTSD Diagnosis	4 (283)[5, 7-9]	Greater loss of PTSD diagnosis RD 0.55 (95% CI, 0.28 to 0.82) All studies favored treatment (3 of 4 studies p<0.05)	Moderate
	Depression Symptoms[b]	4 (283)[5, 7-9]	Reduced depression symptoms Between-group mean differences of individual trials ranged from -11.1 to -8.3 All studies favored treatment (4 of 4 studies p<0.05)	Moderate
Cognitive behavioral therapy-exposure (CBT-exposure)	PTSD Symptoms[a]	13 (885)[3, 10-21]	Reduced PTSD symptoms SMD -1.23 (95% CI, -1.50 to -0.97)	High
		8 (689)[3, 10, 11, 13, 16, 18, 20, 21]	SMD CAPS -1.12 (95% CI, -1.42 to -0.82)	
	Loss of PTSD Diagnosis	6 (409)[3, 13, 14, 16, 17, 21]	Greater loss of PTSD diagnosis RD 0.56 (95% CI, 0.35 to 0.78)	High[c]
	Depression Symptoms[b]	10 (715)[3, 11-15, 18-21]	Reduced depression symptoms SMD -0.76 (95% CI, -0.91 to -0.60)	High

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Cognitive behavioral therapy-mixed (CBT-mixed)	PTSD Symptoms[a]	21 (1,349)[12, 14, 22-40]	Reduced PTSD symptoms SMD -1.01 (95% CI, -1.28 to -0.74)	High[c]
		11 (709)[22, 23, 27-29, 34-39]	SMD -1.24 (95% CI, -1.67 to -0.81)	
	Loss of PTSD Diagnosis	9 (474)[22-24, 31-34, 39, 41]	Greater loss of PTSD diagnosis RD 0.29 (95% CI, 0.17 to 0.40)	High[c]
	Depression Symptoms[b]	15 (929)[12, 14, 22-24, 28, 29, 33, 35-40, 42]	Reduced depression symptoms SMD -0.87 (95% CI, -1.14 to -0.61)	High[c]
Eye movement desensitization and reprocessing (EMDR)	PTSD Symptoms[a]	8 (449)[13, 16, 43-48]	Reduced PTSD symptoms SMD -1.08 (95% CI, -1.82 to -0.35)	Moderate[d]
	Loss of PTSD Diagnosis	7 (427)[13, 16, 43-45, 47, 48]	Greater loss of PTSD diagnosis RD 0.43 (95% CI, 0.25 to 0.61)	Moderate
	Depression Symptoms[b]	7 (347)[13, 43-48]	Reduced depression symptoms SMD -0.91 (95% CI, -1.58 to -0.24)	Moderate
Brief eclectic psychotherapy (BEP)	Loss of PTSD Diagnosis	3 (96)[49-51]	Greater loss of PTSD diagnosis RD of individual studies ranged 0.13 to 0.58 All studies favored treatment (p<0.05)	Low
	Depression Symptoms[b]	3 (96)[49-51]	Reduced depression symptoms Different depression scales used; all 3 studies favored treatment (3 of 3 studies p<0.05)	Low
Imagery rehearsal therapy (IRT)	PTSD Symptoms[a]	1 (168)[52]	Reduced PTSD symptoms Between-group mean difference -21.0; p<0.05	Low
Narrative exposure therapy (NET)	PTSD Symptoms[a]	3 (232)[53-55]	Reduced PTSD symptoms SMD ranged from -1.95 to -0.79 across 3 individual studies (3 of 3 studies p<0.05)	Moderate
	Loss of PTSD Diagnosis	2 (198)[53, 54]	Greater loss of PTSD diagnosis RD of 0.06 and 0.43 in individual studies Both studies favored treatment (1 of 2 studies p<0.05)	Low
Seeking Safety (SS)	PTSD Symptoms[a]	3 (232)[56-58]	Reduced PTSD symptoms SMD of individual trials ranged from -0.22 to 0.04 Two of three trials favored treatment (0 of 3 studies p<0.05)	Low for no difference

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Trauma affect regulation (TAR)	PTSD Symptoms[a]	2 (173)[59, 60]	Reduced PTSD symptoms Between-group mean difference of -17.4 and -2.7 in individual studies Both favored treatment (1 of 2 studies p<0.05)	Low

NOTE: Outcomes graded as insufficient are not included in this table.
[a] SMD from the Clinician-Administered PTSD Scale and other various PTSD symptom scales.
[b] SMD from the Beck Depression Inventory and other various depression symptom scales.
[c] Strength of evidence increased from moderate to high because of additional evidence of efficacy published since prior PTSD review
[d] Strength of evidence increased from low to moderate because of additional evidence of efficacy published since prior PTSD review

CI = confidence interval; N = number of subjects; PTSD = posttraumatic stress disorder; RD = risk difference; SMD = standardized mean difference; SOE = strength of evidence.

Table C. Summary of efficacy and strength of evidence of PTSD pharmacological treatments

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Fluoxetine (SSRI)	PTSD Symptoms[a]	4 (835)[47, 61-63]	Reduced PTSD symptoms SMD -0.28 (95% CI -0.42 to -0.14)	Moderate
	Depression Symptoms[b]	3 (771)[47, 61, 62]	Similar reduction in depression symptoms SMD -0.20 (95% CI -0.40 to 0.00)	Low for no difference[c]
Paroxetine (SSRI)	PTSD Symptoms[a]	2 (348)[64, 65]	Reduced PTSD symptoms SMD of -0.56 to -0.44 in individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
	PTSD Symptom Remission	2 (348)[64, 65]	Greater PTSD symptom reduction RD of 0.13 and 0.19 across 2 individual studies (1 of 2 studies p<0.05)	Moderate
	Depression Symptoms[b]	2 (348)[64, 65]	Reduced depression symptoms SMD ranged from -0.60 to -0.34 across individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
Sertraline (SSRI)	PTSD Symptoms[a]	7 (1,085)[66-72]	Reduced PTSD symptoms SMD -0.20 (95% CI: -0.36 to -0.04)	Low[d]
	Depression Symptoms[b]	7 (1,085)[66-72]	Similar reduction in depression symptoms SMD -0.14 (95% CI: -0.33 to 0.06)	Low for no difference[e]

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Venlafaxine (SNRI)	PTSD Symptoms[a]	2 (687)[69, 73]	Reduced PTSD symptoms SMD of -0.35 and -0.26 for two individual studies	Moderate
	PTSD Symptom Remission	2 (687)[69, 73]	Greater PTSD symptom remission RD of 0.12 and 0.15 across individual studies	Moderate[f]
	Depression Symptoms[b]	2 (687)[69, 73]	Reduced depression symptoms Between-group mean difference of -2.6 and -1.6 across individual studies	Moderate[g]
Prazosin (alpha blocker)	PTSD Symptoms[a]	3 (117)[74-76]	Reduced PTSD symptoms SMD -0.52 (95% CI, -0.90 to -0.14)	Low
Topiramate (anticonvulsant)	PTSD Symptoms[a]	3 (142)[77-79]	Reduced PTSD symptoms SMD ranged from -1.85 to -0.38 across individual studies	Low[h]
Olanzapine (antipsychotic)	PTSD Symptoms[a]	2 (47)[80, 81] 3 (62)[80-82]	Reduced PTSD symptoms SMD of -1.15 and -0.96 across individual studies,[80, 81] both significantly favored treatment, N=47 SMD ranged from -1.15 to 0.89 across individual studies All studies favored treatment (2 of 3 studies p<0.05)	Low
Risperidone (antipsychotic)	PTSD Symptoms[a]	4 (422)[83-86]	Reduced PTSD symptoms SMD -0.26 (95% CI, -0.52 to -0.01)	Low

NOTE: Outcomes graded as insufficient are not included in this table. Insufficient evidence was provided for divalproex (anticonvulsant), tiagabine (anticonvulsant), citalopram (SSRI), all TCAs, buproprion (other second-generation antidepressant [SGA]) and mirtazapine (other SGA). No studies that met inclusion criteria rated as having low or medium risk of bias evaluated lamotrigine (anticonvulsant), any benzodiazepine, desvenlafaxine (SNRI), duloxetine (SNRI), nefazodone (other SGA), or trazodone (other SGA).

[a] SMD from Clinician-Administered PTSD Scale or from various other PTSD symptom scales.
[b] SMD from the Beck Depression Inventory or from various other depression symptom scales.
[c] Strength of evidence changed from moderate in the prior review to low for no difference in the updated review. Only 2 of 3 studies favored treatment, one favored placebo. Imprecision, inconsistency, and effect sizes near the null prompted the change in grade.
[d] Strength of evidence changed from moderate in the prior review to low in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group and findings were imprecise.
[e] Strength of evidence changed from low to low for no difference in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, findings were imprecise, and most individual study estimates were close to the null.
[f] Strength of evidence changed from insufficient to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
[g] Strength of evidence changed from low to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
[h] Strength of evidence changed from moderate in the prior review to low in the updated review. The findings were imprecise, only 1 of 3 individual studies found significant differences between study groups, and the sample sizes were small.

CI = confidence interval; N = number; PTSD = posttraumatic stress disorder; RD = risk difference; SGA = second-generation antidepressant; SMD = standardized mean difference; SNRI = serotonin and norepinephrine reuptake inhibitor; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant

- KQ 3 (Psychological Versus Pharmacological Treatment) Findings
  - Insufficient evidence from a single study examined the comparative effectiveness of a psychological and pharmacological treatment.
- KQ 4 (Adverse Events of Treatments)
  - Most studies did not describe methods used to systematically assess adverse event information.
  - Insufficient evidence was found for all serious adverse event comparisons between and across psychological and pharmacological treatments.
  - When looking at the treatments with at least moderate SOE of benefit, the only adverse event found to have at least moderate SOE was nausea, with venlafaxine.
- Insufficient evidence from only a few studies tested whether efficacy or effectiveness of treatments differed by patient characteristics such as type of trauma exposure, co-occurring condition, or other characteristics (KQs 1a, 2a, 3a).
- For many of our outcomes of interest and interventions of interest (including newer treatments added since our prior review), we did not identify any studies that tested them (KQs 1, 2, 3).
- Contextual Question (CQ) 1a (Components of Efficacious Interventions)
  - One study determined that the most frequently identified components of efficacious PTSD psychological interventions include psychoeducation, coping skills and emotion regulation, cognitive processing and restructuring (i.e., "meaning making"), imaginal exposure, emotions, and memory processing.
- CQ 1b (Fidelity of Efficacious Treatments When Implemented in Clinical Practice Settings)
  - No identified studies tested the degree of fidelity of psychological interventions found to be effective in study settings when implemented in clinical practice settings.

Discussion/Findings in Context: What Does the Review Add to What Is Already Known?

Our review found high SOE of efficacy for CBT-exposure and CBT-mixed treatments and moderate SOE of efficacy for CPT, CT, EMDR, and NET. Among pharmacotherapies, we found moderate SOE of efficacy for fluoxetine, paroxetine, and venlafaxine. Few studies compared treatments with each other, including psychological versus pharmacological treatments, although moderate SOE favors CBT-exposure over relaxation for reduction in PTSD-related outcomes. We did not find sufficient information to comment on whether patients with different types of trauma exposure or other characteristics benefited from a particular type of treatment. For the most part, we found insufficient information about adverse events; insufficient evidence for serious adverse events was found for all of the treatments examined.

Our findings are similar to existing guidelines and systematic reviews that have shown that some psychological therapies and some pharmacological treatments are effective treatments for adults with PTSD. The recently published American Psychological Association (APA) review found evidence to strongly recommend CPT, CT, CBT, prolonged exposure (PE), and to, a slightly lesser degree, recommend EMDR, NET, and brief eclectic psychotherapy (BEP).[87] Each

of these psychological treatments had at least moderate or high strength of evidence of efficacy to reduce PTSD symptoms in this updated review, with the single exception of BEP having insufficient strength of evidence for reduction in PTSD symptoms and low strength of evidence for both loss of PTSD diagnosis and reduction in depression symptoms. The APA group also recommended fluoxetine, paroxetine, venlafaxine, and sertraline, the same four medications recommended in the Department of Defense/Veterans Administration guidelines;[88] this updated review found moderate strength of evidence in support for fluoxetine, paroxetine, venlafaxine as well, with the exception of limited evidence for sertraline (low SOE), driven by heterogeneity in individual study findings.

For the most part, the conclusions made in this update remain unchanged from our prior review published in 2013 on this topic.[89] Additional evidence prompted the increase of a few of the SOE grades for psychological treatments (e.g., CBT-mixed from moderate to high for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms; CBT-exposure from moderate to high for loss of PTSD diagnosis; and EMDR from low to moderate for reduction in PTSD symptoms). Conversely, some of the SOE grades decreased from the last review for some of the pharmacological treatments after reassessing the SOE (fluoxetine from moderate to low for no difference for reduction in depression symptoms, sertraline from moderate to low for reduction in PTSD symptoms and from low [for benefit] to low for no difference for reduction in depression symptoms, and topiramate from moderate to low for reduction in PTSD symptoms), although the SOE changed from insufficient to moderate for loss of PTSD diagnosis and low to moderate for reduction in depression symptoms for venlafaxine (reduction in PTSD symptoms remained at moderate). The SOE moved from insufficient to low for reduction in PTSD symptoms for four treatments—trauma affect regulation (TAR), imagery rehearsal therapy (IRT), prazosin, and olanzapine. Consistent with the prior review, the evidence included in this update yielded mostly insufficient evidence regarding comparative effectiveness and harms associated with treatments of interest. Finally, our searches yielded no evidence of studies that met our inclusion/exclusion criteria that tested any of the newly added treatment types (energy psychology/emotional freedom techniques, and the three atypical antipsychotics, ziprasidone, aripiprazole, and quetiapine).

Despite evidence of benefit of several types of psychological and pharmacological treatments for PTSD, however, clinicians still are uncertain about which treatment to select for individual patients. Our findings suggest that clinicians might need to consider other factors in selecting a treatment for PTSD: patient preference of treatment, whether the patient has care available to them, whether they can afford the treatment, whether they have tried any treatments already, or whether the patient has other co-occurring problems like substance use or depression.

Key Limitations and Research Gaps

Key limitations include the following.

- We did not find studies that met our inclusion/exclusion criteria and studied the efficacy or effectiveness of several types of PTSD treatments such as energy psychology, escitalopram, fluvoxamine, desvenlafaxine, duloxetine, tricyclic antidepressants, other second generation antidepressants, newer antipsychotics (e.g., ziprasidone, aripiprazole and quetiapine), benzodiazepines, and other medications such as naltrexone, cycloserine, and inositol. Of note, none of these interventions are currently approved by the Food and Drug Administration to treat PTSD.

- We did not find many studies of comparative effectiveness that directly compared the benefits of two types of treatments.
- Few studies examined whether particular treatments are better or worse for particular kinds of patients.
- Few studies provided information about adverse events associated with PTSD treatments.

Research gaps include the following.

- Comparing psychological and pharmacological treatments with known benefits in reducing PTSD-related outcomes with each other.
- Examining benefits associated with new PTSD treatments and also the currently used treatments (e.g., energy psychology, escitalopram, fluvoxamine, desvenlafaxine, duloxetine, tricyclic antidepressants, other second generation antidepressants).
- Determining whether certain treatments work better or worse for particular types of patients.
- Designing studies to search and record adverse events for patients enrolled in research studies.

A summary of the review is presented in Table D.

Table D. Summary of review characteristics

Characteristics	Criteria	Summary
Population Included in the Review	Key Inclusion Criteria	Adults ≥18 years of age with PTSD based on any DSM criteria, RCT study designs (or SRs to search references), or non-RCTs with at least 500 subjects for the adverse event KQ (#4)
	Key Exclusion Criteria	Studies with participants <18 years of age, studies without RCT study designs, or studies without at least 500 subjects for KQ4.
Key Topics & Interventions Covered by Review	Key Topics	Interventions
	1. Benefits of psychological treatments; variation in benefits by trauma or other patient characteristics	Brief eclectic psychotherapy, CBT including cognitive restructuring, cognitive processing therapy, exposure-based therapy, coping skills therapy (e.g., stress inoculation therapy, structured approach therapy, relaxation training), psychodynamic therapy, EMDR, interpersonal therapy (IPT), hypnosis or hypnotherapy, neurofeedback, mindfulness-based stress reduction, and energy psychology (including EFT) compared with each other or to an inactive treatment group.
	2. Benefits of pharmacological treatments; variation in benefits by trauma or other patient characteristics	Pharmacological interventions: SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline), SNRIs (desvenlafaxine, venlafaxine, and duloxetine), tricyclic antidepressants (imipramine, amitriptyline, and desipramine), other second-generation antidepressants (bupropion, mirtazapine, nefazodone, and trazodone), alpha blockers (prazosin), atypical antipsychotics (olanzapine, risperidone, ziprasidone, aripiprazole, and quetiapine), benzodiazepines (alprazolam, diazepam, lorazepam, and clonazepam), anticonvulsants/mood stabilizers (topiramate, tiagabine, lamotrigine, carbamazepine, and divalproex) compared to each other or to an inactive treatment group (e.g., placebo).

Characteristics	Criteria	Summary
	3. Comparative benefits of psychological versus pharmacological treatments; variation in benefits by trauma or other patient characteristics	One of the psychological treatments compared with one of the pharmacological treatments of interest.
	4. Adverse events associated with treatments	Any of the psychological or pharmacological treatments of interest.
Timing of the Review	**Beginning Search Date**	May 2012 for treatments included in prior review. No beginning date for treatments newly added to current review.
	End Search Date	September 29, 2017

Important Studies Underway

One trial of mirtazapine (https://clinicaltrials.gov/show/NCT00302107) and one trial of mindfulness based stress reduction (https://clinicaltrials.gov/show/NCT01532999) described as completed in clinicaltrials.gov but findings not yet published.

Introduction

Background

Posttraumatic Stress Disorder

Posttraumatic stress disorder (PTSD) involves a group of symptoms experienced after exposure to a potentially traumatic event. Such symptoms may include re-experiencing the event; avoiding situations that trigger memories of the event; experiencing increased negative feelings and beliefs; experiencing feelings of hyperarousal such as irritability, agitation, anger, or being on alert; and experiencing various combinations of these indicators.[90] The traumatic event (stressor) must involve either witnessing an actual or threatened death or serious injury or other threat to one's physical integrity or witnessing an event that involves death, injury, or a threat to the physical integrity of another person. Alternatively, the event must involve learning about unexpected or violent death, serious harm, or threat of death or injury experienced by a family member or other close associate.[90]

Some traumatic events that are directly experienced include military combat, violent personal assault, being taken hostage, a terrorist attack, torture, natural or manmade disasters, and being diagnosed with a life-threatening illness.[91] They can also comprise relational trauma such as sexual, physical, and emotional abuse and domestic violence. Not all people exposed to a potentially traumatic event, however, go on to develop posttraumatic stress symptoms and PTSD.

According to one meta-analysis of 35 longitudinal study samples, 28.8 percent (range: 3.1% to 87.5%) of adults exposed to one or more potentially traumatic events meet criteria for PTSD within 1 month of trauma exposure, and 17.0 percent continue to meet criteria for PTSD 12 months following exposure (range: 0.6% to 43.8%).[92] PTSD is also highly comorbid with other psychiatric disorders; data from epidemiologic studies indicate that a vast majority of individuals with PTSD have a co-occurring disorder, most notably substance use disorders, mood disorders, anxiety disorders, and suicidality.[93, 94]

Individuals may vary in their response to various PTSD treatments. Moderators of treatment effectiveness include sociodemographic and health characteristics, such as racial and ethnic minorities; gender; types, severity, or chronicity of PTSD symptoms; and coexisting conditions. Employment factors such as current or past military or first responder service may also influence effectiveness of interventions. Finally, refugees and disaster victims may differ in their outcomes of PTSD therapies.

In the Diagnostic and Statistical Manual of Mental Disorders, fifth edition (DSM-5),[91] PTSD criteria are analogous to, but not exactly the same as, the prior DSM-IV criteria.[90] In DSM-5, PTSD has four symptom clusters: (1) intrusion (similar to the re-experiencing criterion in DSM-IV), (2) avoidance (without inclusion of numbing symptoms, as in DSM-IV), (3) negative alterations in cognition and mood, and (4) alterations in arousal and reactivity (similar to increased arousal in DSM-IV). Table 1 summarizes these criteria and major changes between the two DSM volumes. The severity of the symptoms of PTSD can be measured in clinical or research settings using a number of validated scales that typically result in a numeric score that roughly corresponds with the intensity, number, duration, subjective distress, or impact of symptoms on functioning.

Note: The reference list follows the appendixes.

Table 1. Diagnostic criteria for posttraumatic stress disorder

DSM-IV Criterion	DSM-5 Criterion	Summary of Major Changes in DSM-5
Criterion A: Traumatic event that involved: actual or threatened death, serious injury, OR threat to physical integrity AND Intense response of fear, helplessness, or horror	Criterion A: Traumatic event as defined by: direct exposure to, witnessing indirectly (by learning a close friend or close relative was exposed), OR repeated/extreme indirect exposure in the course of professional job (not through media)	Changes to wording of traumatic event exposure specification DROPPED Intense response of fear, helplessness, or horror criterion
Criterion B: Re-experiencing symptoms (1 or more): Intrusive recollections of events Recurrent distressing dreams of the event Acting or feeling as if the traumatic event were recurring Distress at internal or external reminders of the trauma Physiological reaction to internal or external reminders	Criterion B: Intrusion symptoms (1 or more): Recurrent, intrusive memories Traumatic nightmares Flashbacks Intense/prolonged distress after exposure Physiological reactivity upon exposure to cues	New title of criterion Changes to wording of criterion
Criterion C: Persistent avoidance and numbing (3 or more): Avoidance of thoughts, feelings, or conversations associated with trauma Avoidance of activities, places, or people that arouse recollections of trauma Failure to recall an important aspect of trauma Loss of interest or participation in significant activities Detachment from others Restricted range of affect Lost sense of the future	Criterion C: Persistent effortful avoidance of distressing trauma-related stimuli (1 or more): Trauma-related thoughts/feelings Trauma-related external reminders Criterion D: Negative cognitions/mood (2 of 7) Inability to recall key features of the trauma Negative beliefs about oneself, the world Distorted blame of self, others Persistent negative trauma-related emotions Diminished interest Feeling alienated, detachment/estrangement Constricted affect	Split avoidance and negative sequelae into 2 criteria Changes to wording of specific criterion
Criterion D: Hyperarousal (2 or more): Difficulty falling or staying asleep Irritability or outburst of anger Difficulty concentrating Hypervigilance Exaggerated startle response	Criterion E: Alterations in arousal and reactivity (2 or more): Irritable or aggressive behavior Self-destructive/reckless behavior Hypervigilance Exaggerated startle response Problems in concentration Sleep disturbance	New title of criterion Changes to wording of criterion Added self-destructive/reckless behavior
Criterion E: Duration of disturbance Duration of disturbance symptoms is more than 1 month	Criterion F: Duration of disturbance Duration of disturbance symptoms is more than 1 month	None
Criterion F: Clinically significant distress or impairment Duration of disturbance symptoms is more than 1 month	Criterion G: Clinically significant distress or impairment Duration of disturbance symptoms is more than 1 month	None

DSM-IV Criterion	DSM-5 Criterion	Summary of Major Changes in DSM-5
Criterion G: Exclusion criteria	Criterion H: Exclusion criteria	None
Symptoms are not due to medication, substance use, or other illness	Symptoms are not due to medication, substance use, or other illness	

DSM-IV = Diagnostic and Statistical Manual of Mental Disorders, 4th Edition; DSM-5 = Diagnostic and Statistical Manual of Mental Disorders, 5th Edition.

Prevalence

The National Comorbidity Survey—Replication conducted between 2001 and 2003 estimated lifetime prevalence of PTSD based on DSM-IV criteria among all adults in the United States as 6.8 percent (9.7% in women and 3.4% in men) and current 12-month prevalence as 3.6 percent (5.2% in women and 1.8% in men).[94] More recently collected data from the National Epidemiologic Survey on Alcohol and Related Conditions in 2012–2013 determined a lifetime prevalence of PTSD based on DSM-5 criteria among adults in the United States to be 6.1 percent (4.7% were determined to have past year [12-month] prevalence).[93, 95] Military personnel have an elevated risk for exposure to trauma and, thus, an elevated risk for a PTSD diagnosis. Estimates from the National Vietnam Veterans Readjustment Survey found a DSM-IV lifetime PTSD prevalence estimate of 18.7 percent and a current PTSD prevalence estimate of 9.1 percent among Vietnam veterans.[96] Surveys of military personnel returning from operations in Afghanistan and Iraq have yielded a wide range of PTSD estimates—for example, 12.6 percent of U.S. men who fought in Iraq and 6.2 percent of U.S. men who fought in Afghanistan. It is estimated that approximately 20 percent of female veterans of the conflicts in Iraq or Afghanistan suffer from PTSD in their lifetimes.[97]

Burden

The significant social, personal, and economic costs of PTSD exemplify the importance of this systematic review.[98] People affected by PTSD have high rates of psychiatric comorbidity and have problems with functioning (e.g., family, work, social). They also tend to suffer adverse consequences over the life course such as difficulties with educational attainment, work earnings, marriage attainment, and child rearing.[98] Almost one-half (42.6%) of adults with PTSD do not get mental health treatment.[99] Among those who do, only 40.4 percent get minimally adequate treatment.[99] Evidence-based guidelines define such therapy as receiving either appropriate pharmacotherapy for 2 or more months for the focal disorder plus more than four visits to any type of physician or eight or more psychotherapy visits with any health care or human services professional lasting an average of 30 minutes or more.[99] Although studies have shown that about 92 percent of adults with lifetime PTSD eventually achieve remission, the median time to remission is 14 years.[100]

Treatment Strategies

Early diagnosis and appropriate treatment of people with PTSD are critical to reducing the duration and severity of symptoms, associated functional impairment, and associated costs.[101] Treatment guidelines typically include guidance about both psychological and pharmacological types of treatments[87, 88, 102-106] No clearly defined “preferred” approach to managing PTSD exists. However, many of the existing treatment guidelines support the use of trauma-focused psychological treatments for adults with PTSD, and most guidelines recognize at least some

benefit of pharmacological treatments for PTSD. Some guidelines suggest trauma-focused psychological treatments over pharmacological treatments as a preferred first step and medications as an adjunct or a next-line treatment.[104, 105]

Practical considerations and patient preferences may guide treatment decisions. For example, the selection of an initial treatment plan may depend on whether the clinician can prescribe medications or provide psychotherapy. Finally, a patient's coexisting physical or other mental health conditions (e.g., depression, anxiety, serious mental illness, eating disorders, chronic pain, gastrointestinal symptoms, or drug or alcohol use disorders) may influence the type of treatment selected.[104, 105]

Psychological Interventions

Specific psychological interventions have been studied for the treatment of PTSD. They include cognitive behavioral therapy (CBT) such as cognitive interventions, coping skills therapies, and exposure-based therapy; eye movement desensitization and reprocessing (EMDR); and other forms of individual and group therapies. Appendix A displays additional details about some commonly used psychological interventions to treat PTSD. The application of these treatments seeks to minimize the intrusion, avoidance, and hyperarousal symptoms of PTSD via some combination of learning and conditioning, working to change thought patterns and beliefs, re-experiencing and working through trauma-related memories and emotions, and teaching better methods of managing trauma-related stressors.

Pharmacological Interventions

Currently, the U.S. Food and Drug Administration has approved only paroxetine and sertraline for treating patients with PTSD. Other pharmacological agents that have been used as therapies for PTSD patients include the following: other selective serotonin reuptake inhibitors; serotonin and norepinephrine reuptake inhibitors; tricyclic antidepressants; other second-generation antidepressants; atypical antipsychotics; anticonvulsants and mood stabilizers; adrenergic agents; benzodiazepines; and other pharmacological agents such as naltrexone, cycloserine, and inositol.[107, 108] Specific medications within these drug classes that have been studied or used in treating PTSD are listed in Table 2 in the Methods section below.

Outcomes

The primary outcome in PTSD treatment is symptom reduction. Authors often categorize symptom reduction into whether each respondent meets the remission criteria at posttreatment and followup assessments. Some studies also include loss of PTSD diagnosis as an outcome, defined as no longer meeting all PTSD criteria for number or type of requisite symptoms and/or functional impairment. Some commonly used instruments used to measure outcomes, which include both self-reported and clinician-administered assessments, are listed in Appendix B of this report. These instruments contain items assessing some or all of either DSM-IV or DSM-5 symptoms of PTSD; these cover domains such as exposure to a traumatic event, re-experiencing of symptoms, persistent arousal and numbing, and hyperarousal. Some instruments can be administered in as little as 5 minutes, whereas others take an hour or more to complete. These instruments are reliable and valid; some have acceptable psychometric properties across multiple subpopulations (e.g., active duty military personnel, veterans, trauma survivors, general population). Other outcomes often assessed in clinical practice include prevention or reduction of coexisting medical or psychiatric conditions, such as depressive symptoms, anxiety symptoms,

or problematic substance use. Yet other end results of care can include improved quality of life, reduced functional limitations or disability, and ability to return to work or return to active duty.

Scope and Key Questions

Scope of the Review

Summary of Existing Clinical Practice Guidelines

Various guidelines and systematic reviews have yielded contradictory conclusions and recommendations regarding the comparative effectiveness and harms of psychological and pharmacological treatments for PTSD. In general, some guidelines identify psychological treatments over pharmacological treatments as the preferred first-line treatment, with medication to be used adjunctively or as a second option when psychotherapy does not adequately decrease symptoms and associated impairment. Other guidelines do not differentiate first-line versus other treatments. Although various evidence-based approaches to treatment exist, clinical uncertainty remains about which treatment to select for which patients. Furthermore, clinicians need to consider patient treatment preferences in treatment selection, given that selecting a treatment a patient does not prefer or value can affect treatment use, dropout rates, adherence to therapy, and therapeutic response. Numerous organizations have produced guidelines for treating PTSD: the American Psychiatric Association, the American Psychological Association, the U.S. Department of Veterans Affairs/U.S. Department of Defense, the National Institute for Health and Care Excellence in the United Kingdom, the National Health and Medical Research Council, the International Society for Traumatic Stress Studies, the American Academy of Child and Adolescent Psychiatry, Health and Medicine Division of the National Academies, and the World Health Organization.

The organizations and guideline developers used different methods, which may contribute to the variation in recommendations regarding the types of treatments and/or the order in which treatments should be used. Some guidelines are based on rigorous systematic reviews; others are based on expert consensus and less structured literature reviews. Differences in systematic review findings also may relate to the application of various rating systems to assess the strength of evidence (SOE) of the research findings. These methodological differences may lead, in part, to different syntheses of findings and overall conclusions, ultimately leading to variations in recommendations. Where one report found evidence to suggest efficacy of a particular treatment, another report deemed the underlying evidence inadequate to address efficacy and, therefore, was unable to make a recommendation.

Summary of Previous Systematic Review

The prior PTSD systematic review conducted for the Agency for Healthcare Quality and Research[89] concluded that several psychological interventions (exposure therapy, cognitive processing therapy, cognitive therapy, CBT-mixed therapies, EMDR, and narrative exposure therapy) and pharmacological treatments (fluoxetine, paroxetine, sertraline, topiramate, and venlafaxine) have at least moderate SOE in support of their efficacy. The review found sparse evidence of head-to-head comparisons between these interventions, however, limiting conclusions about comparative effectiveness.

Overall, the review found insufficient evidence of whether the efficacy or comparative effectiveness of different treatment approaches varied by patient characteristics or type of trauma

experienced. Likewise, the review found limited evidence about adverse effects across different intervention types.

In addition to the need to update systematic reviews every few years [109] when areas of clinical uncertainty remain, this updated review expands the scope of treatment types examined. Specifically, we include one psychological intervention not examined in the prior review, energy psychology (also known as emotional freedom techniques), and three atypical antipsychotics (namely, ziprasidone, aripiprazole, and quetiapine). We also assessed newer studies that might have used DSM-5 criteria to assess PTSD diagnosis to help shed light on the implications of the criteria change on the efficacy of treatments. No new studies, however, used DSM-5 criteria to assess PTSD. The change in criteria from DSM-IV to DSM-5 requires additional research; the field has yet to determine the impact of the changes. Synthesis of new and existing evidence addresses the uncertainties noted in the conclusions of our earlier systematic review about ways to improve the care of those with PTSD and to reduce the variation in existing treatment guidelines.

Key Questions

KQ 1: What is the comparative effectiveness of different psychological treatments for adults diagnosed with PTSD?

> **KQ 1a**. How does comparative effectiveness vary by patient characteristics or type of trauma experienced?

KQ 2: What is the comparative effectiveness of different pharmacological treatments for adults diagnosed with PTSD?

> **KQ 2a.** How does comparative effectiveness vary by patient characteristics or type of trauma experienced?

KQ 3: What is the comparative effectiveness of different psychological treatments and pharmacological treatments for adults diagnosed with PTSD?

> **KQ 3a.** How does comparative effectiveness vary by patient characteristics or type of trauma experienced?

KQ 4: What adverse events (AEs) are associated with treatments for adults diagnosed with PTSD?

Contextual Questions

Contextual Question (CQ) 1a. What are the components of effective psychological treatments (e.g., frequency or intensity of therapy and/or aspects of the therapeutic modality)?

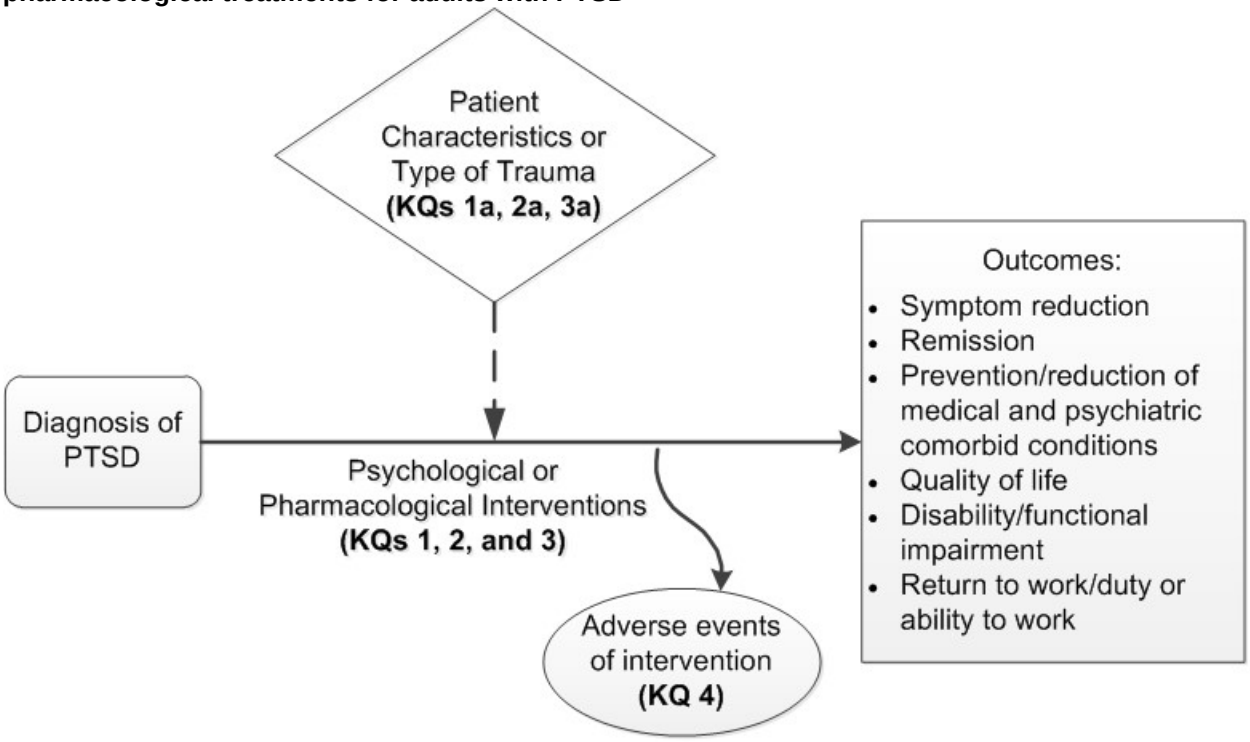
CQ 1b. For psychological interventions that are effective in trial settings, what is the degree of fidelity when implemented in clinical practice settings?

Analytic Framework

Figure 1 depicts the analytic framework for the comparative effectiveness of psychological treatments and pharmacological treatments for adults with PTSD. We describe details of population, intervention, comparators, outcomes, timing, and setting in the Methods section

below. Beginning with a population of adults diagnosed with PTSD, the figure illustrates the effect of psychological and pharmacological interventions on outcomes of PTSD. Those important outcomes include symptom reduction and remission, prevention or reduction of medical and psychiatric comorbid conditions, quality of life, disability or functional impairment, and ability to work or ability to return to either work or duty (KQ 1, KQ 2, and KQ 3). Patient characteristics and type of trauma are explored as potential moderators of these interventions in KQ 1a, KQ 2a, and KQ 3a. Finally, KQ 4 examines the AEs of these interventions.

Figure 1. Analytic framework for the comparative effectiveness of psychological treatments and pharmacological treatments for adults with PTSD



KQ = Key Question; PTSD = posttraumatic stress disorder.

Organization of This Report

We describe our methods next and then present our key findings in the Results chapter. In the Discussion chapter, we explore the implications of our findings and examine the limitations of the evidence base and this review, clarify gaps in the knowledge base, and offer recommendations for future research. References follow the appendixes.

The main report has several appendixes, as follows: A, intervention types; B, outcome measures and instruments; C, search strategies; D, excluded studies; E, risk of bias tables; F, evidence tables; G, high risk of bias study documentation; H, meta-analysis forest plots; I, strength of evidence; J, expert guidance and review.

Methods

The methods for this systematic review follow the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews* from the Agency for Healthcare Research and Quality (AHRQ).[110] The PRISMA (Preferred Reporting Items for Systematic Reviews and Meta-Analyses) checklist facilitated the preparation and reporting of the systematic review.[111]

Topic Refinement and Review Protocol

Our Evidence-based Practice Center (EPC) developed this topic and Key Questions (KQs) originally through a public process. AHRQ staff refined the topic further for this update of our previously conducted review.

We drafted a protocol for the update of the systematic review. The final protocol can be found on the Effective Health Care Web site (https://effectivehealthcare.ahrq.gov/topics/ptsd-adult-treatment-update/research-protocol); and registered on PROSPERO (Registration number: CRD42017075672).

Literature Search Strategy

Search Strategy

We systematically searched, reviewed, and analyzed the scientific evidence gathered to help answer our KQs. We began with a focused MEDLINE® search for eligible interventions using a combination of medical subject headings (MeSH®) and title and abstract keywords, limiting the search to human-only studies (Appendix C) (from inception through September 29, 2017). We also searched the Cochrane Library, the Cochrane Clinical Trials Registry, PsycINFO, the Cumulative Index to Nursing and Allied Health Literature, and the Published International Literature on Traumatic Stress database using analogous search terms. These searches included randomized controlled trials (RCTs), controlled clinical trials, and systematic reviews. We selected these databases based on preliminary searches and consultation with content experts. We conducted quality checks to ensure that the search identified known studies (e.g., studies included in the previous review).

Because the prior review's literature searches ended in May 2012, we searched the literature published since January 2012 to account for lags in indexing published studies. An experienced librarian familiar with systematic reviews designed and conducted all searches in consultation with the review team. We did not include studies testing energy psychology interventions/ emotional freedom techniques (EFT) or those testing the efficacy of the atypical antipsychotics ziprasidone, aripiprazole, or quetiapine as part of the prior review. Thus, for this update, we conducted a separate search using these terms crossed with posttraumatic stress disorder (PTSD) terms (see Appendix C for full list of terms); in addition, we did not impose a publication date limit on this separate search to allow us to capture all pertinent studies ever published. We searched the grey literature for unpublished studies relevant to this review and included studies that met all the inclusion criteria and contained enough methodological information for assessing internal validity (quality or risk of bias). Sources of grey literature included ClinicalTrials.gov. We did not receive any pharmaceutical companies' dossiers (for pharmacotherapies of interest) or scientific evidence and data in response to notice requests placed in the *Federal Register*.

To answer the Contextual Questions (CQs), we searched our included psychological treatment studies, the reviews captured by our search, and the gray literature that discussed

components of effective psychological treatments. Our interest was in factors such as frequency or intensity of therapy and aspects of the therapeutic modality. We flagged studies of interest during our abstract review and full-text review. In addition, for psychological interventions determined to be efficacious in trial settings, we looked for evidence that described the degree of fidelity to protocol when interventions were implemented into clinical practice. We discuss the CQ evidence identified by our searches in the Discussion section to provide context to our main report findings.

Inclusion and Exclusion Criteria

We specified and refined our inclusion and exclusion criteria based on the populations, interventions, comparators, outcomes, timing, and settings (PICOTS) identified for this updated review (Table 2).

Table 2. Inclusion/exclusion criteria for psychological and pharmacological treatments for adults with posttraumatic stress disorder

PICOTS	Inclusion	Exclusion
Population	Adults 18 years or older with a majority having PTSD based on any DSM diagnostic criteria Subgroups of interest (KQs 1a, 2a, 3a) include those distinguished by • patient characteristics: gender, age, race or ethnicity, comorbid mental and physical health conditions, employment types requiring trauma exposure (e.g., first responders), severity of trauma experienced, different symptoms of PTSD, dissociation, psychosis, PTSD symptom chronicity or severity • type of trauma experienced: military/combat, natural disaster, war, political instability, relational problems relating to, for example, physical, emotional, or sexual abuse or exposure to domestic violence, repeat victimizations, or cumulative	All other
Intervention	Psychological interventions: Brief eclectic psychotherapy, CBT including cognitive restructuring, cognitive processing therapy, exposure-based therapy, coping skills therapy (e.g., stress inoculation therapy, structured approach therapy, relaxation training), psychodynamic therapy, EMDR, interpersonal therapy (IPT), neurofeedback (NF), mindfulness-based stress reduction (MBSR), hypnosis or hypnotherapy, and energy psychology (including EFT) Pharmacological interventions: SSRIs (citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline), SNRIs (desvenlafaxine, venlafaxine, and duloxetine), tricyclic antidepressants (imipramine, amitriptyline, and desipramine), other second-generation antidepressants (bupropion, mirtazapine, nefazodone, and trazodone), alpha blockers (prazosin), atypical antipsychotics (olanzapine, risperidone, ziprasidone, aripiprazole, and quetiapine), benzodiazepines (alprazolam, diazepam, lorazepam, and clonazepam), anticonvulsants/mood stabilizers (topiramate, tiagabine, lamotrigine, carbamazepine, and divalproex)	Complementary and alternative medicine approaches Psychological or pharmacological interventions not listed as included

PICOTS	Inclusion	Exclusion
Comparator	KQ 1 (1a): Psychological interventions listed above compared with one another, waiting list assignment, usual care (as defined by the study), no intervention, or sham (an inactive treatment intended to mimic a therapy in a trial as closely as possible) KQ 2 (2a): Pharmacological interventions listed above compared with one another or placebo KQ 3 (3a): Psychological interventions listed above compared with pharmacological interventions listed above KQ 4: Any intervention listed above	All other comparisons
Outcomes	KQs 1–3: PTSD symptom reduction (see Appendix A for a list of measures), including categorical reduction of symptoms below a prespecified threshold (remission) or loss of PTSD diagnosis, prevention or reduction of comorbid medical or psychiatric conditions (e.g., coronary artery disease; depressive symptoms; anxiety symptoms; suicidal ideation/plans/attempts; and substance use, abuse, or dependence), quality of life, disability or functional impairment, return to work or active duty status KQ 4: Overall and specific AEs (e.g., disturbed sleep, increased agitation, sedation, weight gain, metabolic side effects, and mortality), withdrawals due to AEs	All other outcomes
Time frame	All publication years. New studies, obtained by searching databases from 2012 to the present to identify studies meeting the review criteria published since the last update, added to studies included in prior report that continue to meet the new review criteria. At least 4 weeks of treatment	Less than 4 weeks of treatment
Settings	Outpatient and inpatient primary care or specialty mental health care; community settings (places of worship, community health centers, rape crisis centers)	Other settings
Study design	KQs 1–3: RCTs of any sample size, systematic reviews (for references) KQ 4: Adverse event data from trials for KQs 1–3, systematic reviews and meta-analyses (for references), nonrandomized controlled trials, prospective cohort studies with an eligible comparison group and a sample size of at least 500,[a] case-control studies with a sample size of at least 500[a]	All other designs and studies using included designs that do not meet the sample size criterion
Language	Studies published in English[b]	Studies published in languages other than English

[a] Observational studies that compare the effectiveness of various treatments for PTSD have a very high risk of selection bias and confounding. We feel that the results should not be used to draw conclusions about efficacy or effectiveness. For KQ 4, we chose a sample size cutoff of 500 for prospective cohort studies and case-control studies for several reasons: (1) the topic refinement process done for the prior review that we are currently updating found a large number of trials in this field, and it was determined that increasing comprehensiveness by reviewing all possible observational studies that present harms was outweighed by the potential decreased quality/increased risk of bias of these studies; (2) the threshold of 500 will ensure the inclusion of only large observational studies with the lowest potential risk of bias to supplement the trial literature; and (3) the Technical Expert Panel of the prior project supported this approach.

[b] Owing to limited time and resources, we included only studies published in English.

CBT = cognitive behavioral therapy; DSM = Diagnostic and Statistical Manual; EFT = emotional freedom techniques; EMDR = eye movement desensitization and reprocessing; IPT = interpersonal therapy; KQ = Key Question; MBSR = mindfulness-based stress reduction; NF = neurofeedback; PICOTS = populations, interventions, comparators, outcomes, timing, and setting; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; SNRI = serotonin and norepinephrine reuptake inhibitor; SSRI = selective serotonin reuptake inhibitor.

Study Selection

Two trained research team members independently reviewed all titles and abstracts identified through searches for eligibility against our inclusion and exclusion criteria. Studies marked for

possible inclusion by either reviewer underwent a dual, independent full-text review. For studies without adequate information to determine inclusion or exclusion, we retrieved the full text and then made the determination. We also reevaluated all articles included in the prior PTSD systematic review for inclusion based on the inclusion and exclusion criteria of this updated review. We tracked all results in an EndNote® bibliographic database (Thomson Reuters, New York, NY).

We retrieved and reviewed the full text of all articles included during the title and abstract review phase. Two trained team members independently reviewed each full-text article for inclusion or exclusion based on the eligibility criteria described above. If both reviewers agreed that a study did not meet the eligibility criteria, we excluded the study. If the reviewers disagreed, conflicts were resolved by discussion and consensus or by consulting a third member of the review team. All results were tracked in an EndNote database.

We also recorded the main reason that each excluded full-text publication did not satisfy the updated eligibility criteria (Appendix D). This permitted us to compile a comprehensive list of such studies.

Data Extraction

We pretested abstraction forms and trained abstractors on a set of 10 studies. For studies that met our inclusion criteria, we abstracted relevant information into evidence tables. We designed data abstraction forms to gather pertinent information from each article, including characteristics of study populations, settings, interventions, comparators, study designs, methods, and results. Trained reviewers extracted the relevant data from each included article into the evidence tables. A second member of the team reviewed all data abstractions for completeness and accuracy.

Quality (Risk of Bias) Assessment of Individual Studies

To assess the risk of bias of RCTs, we used the same criteria applied in the 2013 AHRQ review by Jonas and colleagues,[89] based on the AHRQ *Methods Guide for Comparative Effectiveness Reviews.*[109] We added a question to the prior risk of bias assessment tool to indicate whether authors reported all prespecified outcomes. The ROBINS-1[112] tool (for observational studies) and the Cochrane RCT tool[113] (for RCTs) contain similar criteria as those used for this updated review.

For both RCTs and observational studies, in addition to questions addressing treatment fidelity and whether authors reported all prespecified outcomes, our evaluation included questions to determine selection bias, confounding, performance bias, detection bias, and attrition bias. Concepts covered included adequacy of randomization (for RCTs only), similarity of groups at baseline, masking, attrition, indication of whether authors used intention-to-treat analysis, methods for handling dropouts and missing data, treatment fidelity, and validity and reliability of outcome measures.[110] Appendix E shows risk of bias assessments for each study that met inclusion criteria.

Two independent reviewers randomly sampled 10 studies in the 2013 review and reassessed risk of bias using the full set of questions that included the new item assessing reporting of all prespecified outcomes. Because ratings were consistent between original and re-reviewers, we accepted the ratings of each study included in the prior review and rated risk of bias only of newly identified studies. Two independent reviewers assigned these ratings for each new study, and they resolved any disagreements by discussion and consensus or by consulting a third member of the team.

A study rated as “low” has the least bias, and its results are considered valid. A “medium” rating indicates the study has susceptibility to some bias but probably not sufficient to invalidate its results. A study rated as “high” risk of bias has significant bias (stemming from, e.g., serious errors in design or analysis) that may invalidate its results. In general, we gave a low risk of bias rating to studies that met all criteria. Medium ratings were given to studies that presumably fulfilled at least some quality criteria but did not report their methods sufficiently to answer all our questions. We gave a rating of high to studies that had one or more fatal flaws (defined as a methodological shortcoming that leads to a very high risk of bias) in one or more categories. We did not include these studies in qualitative or quantitative analyses used to determine the findings of our review. Appendix F lists each study rated high risk of bias that met the inclusion criteria, along with details on the consistency between the findings from the studies rated as having high risk of bias with those from studies rated as having low or medium risk of bias for each intervention, comparator, and outcome combination reported.

Data Synthesis

We summarized study findings in narrative form; we also created summary tables that tabulate the important features of the study populations, design, intervention, outcomes, settings, and results. All new qualitative and quantitative analyses synthesize studies from the 2013 systematic review that continued to meet criteria of the updated review with those newly identified as a single body of evidence. Appendix G contains evidence tables for all included studies rated low or medium risk of bias.

We carefully considered each body of evidence to determine if findings could be quantitatively pooled as per recent guidance.[110] If we found three or more studies with low heterogeneity for a comparison of interest, we performed meta-analysis of the common outcomes from those studies using the metan procedure in Stata and a Dersimonian-Laird estimator based on recent recommendations.[114] We also conducted network meta-analysis using the network procedure in Stata[115] to compare the pharmacological interventions with each other when we identified at least three studies with low heterogeneity that tested the same intervention with a common comparator (e.g., inactive comparator or active comparator naming a specific intervention) after examining the studies entered as inputs to the network meta-analysis for transitivity. For all analyses, we used random-effects models to estimate pooled or comparative effects.[110] For continuous outcomes, we report the standardized mean difference in pre- to postintervention scores between groups when analyses included studies with the same outcome assessments and standardized mean differences when pooling two or more assessment tools. For dichotomous outcomes such as remission and loss of PTSD diagnosis, we report the risk difference between groups. If studies were determined to have moderate heterogeneity, we required five studies to perform meta-analysis of the common outcomes. We did not conduct a network meta-analysis for the psychological interventions because of great levels of heterogeneity in the interventions tested and, to a lesser extent, the comparators used in these studies.

In general, to determine whether quantitative analyses were appropriate, we assessed the clinical and methodological heterogeneity of the studies under consideration following established guidance.[110] When bodies of evidence consisted of three studies with low heterogeneity that tested the efficacy or comparative effectiveness of the same intervention (and same comparator when examining comparative effectiveness studies), quantitative meta-analysis was performed when the clinical and methodological heterogeneity of the studies were

determined to be insignificant. Similarly, meta-analyses were performed when at least five studies of moderate clinical and methodological heterogeneity tested the efficacy or comparative effectiveness of the same intervention (and same comparator when examining comparative effectiveness studies). The judgment of heterogeneity was done by qualitatively assessing the PICOTS of the included studies, looking for similarities and differences. When we could conduct quantitative syntheses (i.e., meta-analysis), we assessed statistical heterogeneity in effects between studies by calculating the chi-squared statistic and the I^2 statistic (the proportion of variation in study estimates attributable to heterogeneity). The importance of the observed value of I^2 depended on the magnitude and direction of effects.

If we include any meta-analyses with considerable statistical heterogeneity in this report, we provide an explanation for doing so, considering the magnitude and direction of effects. When quantitative analyses are not appropriate (because of, e.g., heterogeneity, insufficient numbers of similar studies, or insufficiency or variation in outcome reporting), we synthesize data qualitatively.

Forest plots depict the findings of all quantitative meta-analyses (bodies of evidence with five or more studies or three or four studies with low heterogeneity testing the same intervention). In some instances, when the number of studies was low or the level of heterogeneity for bodies of evidence with three or four studies was high, forest plots are presented without displaying a pooled estimate.

Strength of the Body of Evidence

We graded the strength of evidence (SOE) based on the guidance established for AHRQ's EPC Program.[116, 117] Senior members of the review team (including at least one subject matter expert and one methodologist) graded the SOE.

Developed to grade the overall strength of a body of evidence, this approach incorporates five key domains: risk of bias (includes study design and aggregate quality), consistency, directness, precision of the evidence, and reporting bias. It also considers other optional domains that may be relevant for some scenarios, such as a dose-response association, plausible confounding that would decrease the observed effect, and strength of association (magnitude of effect).

Table 3 describes SOE grades. Grades reflect the strength of the body of evidence to answer KQs on the comparative effectiveness, efficacy, and harms of the interventions in this review. Two reviewers assessed each domain for each key outcome; they resolved any differences by consensus discussion. We graded the SOE for all outcomes of interest. Primary outcomes directly associated with PTSD symptoms and associated impairment included decrease in PTSD symptoms, remission (decrease in symptoms below an author-set threshold), and loss of diagnosis (which required the loss of specific number and types of symptoms, timing of symptoms, and loss of associated impairment requisite for a PTSD diagnosis). Other outcomes not directly associated with PTSD symptoms or associated impairment, but still important to overall functioning, included comorbid depression, anxiety, and substance use symptoms; quality of life; disability or functional impairment; and adverse events.

Appendix I displays SOE tables for each study.

Table 3. Definitions of the grades of overall strength of evidence[37]

Grade	Definition
High	High confidence that the evidence reflects the true effect. Further research is very unlikely to change our confidence in the estimate of effect.
Moderate	Moderate confidence that the evidence reflects the true effect. Further research may change our confidence in the estimate of the effect and may change the estimate.
Low	Low confidence that the evidence reflects the true effect. Further research is likely to change our confidence in the estimate of the effect and is likely to change the estimate.
Insufficient	Evidence either is unavailable or does not permit estimation of an effect.

Applicability

We assessed the applicability of individual studies, as well as the applicability of the body of evidence following guidance from the *Methods Guide for Effectiveness and Comparative Effectiveness Reviews*.[110] For individual studies, we examined conditions that may have limited applicability based on the PICOTS structure, such as age of enrolled population, index type of trauma experienced (including military-related or combat-related trauma), severity of trauma, and setting of enrolled populations (e.g., hospital, community health center). We also considered whether findings of intervention studies that used Diagnostic and Statistical Manual of Mental Disorders, 4th edition criteria for PTSD could be extended to individuals meeting Diagnostic and Statistical Manual of Mental Disorders, fifth edition criteria for PTSD.

Peer Review and Public Commentary

Experts in PTSD treatment were invited to provide external peer review of the draft systematic review. AHRQ staff, Patient-Centered Outcomes Research Institute staff, and an Associate Editor reviewed the draft systematic review before it went out for peer review. The EPC Associate Editors are leaders in their respective fields and are actively involved as directors or leaders at their EPCs. Their role is to assess adherence to established methodology and guidelines for EPC-based research. The draft report was posted on the AHRQ Web site from November 15, 2017, to December 29, 2017, to elicit public comment. We revised the report in response to reviewer comments, expanded the analysis strategies, and noted any resulting revisions to the text in the "Disposition of Comments Report." This disposition report will be made available 3 months after the final systematic review is posted on the AHRQ Web site. Additional details about the expert guidance and review are provided in Appendix J.

Results

This section contains findings organized by Key Question (KQ) and grouped by interventions (i.e., by type of psychological treatment or by drug class). For each KQ, we first give the key points and then proceed with a more detailed synthesis of the literature.

KQ 1 addresses the efficacy of psychological treatments and their comparative effectiveness with each other. For each type of psychotherapy, we first address efficacy by evaluating studies with inactive comparison groups (e.g., wait-list or treatment as usual/usual care). We group treatment-as-usual and usual-care comparators together when we synthesize findings and label the combined group "usual care" throughout the report. By the term *inactive*, we mean comparators that do not involve a specific therapeutic intervention. We then proceed to address comparative effectiveness of a given psychotherapy by evaluating studies with active comparison groups (i.e., head-to-head studies involving other specific psychological interventions).

KQ 2 addresses efficacy of pharmacological treatments and their comparative effectiveness with each other. As with KQ 1, we first address efficacy for each type of pharmacotherapy by evaluating studies with inactive comparators (e.g., placebo). We then proceed to address comparative effectiveness by evaluating head-to-head pharmacological studies (i.e., drug vs. drug).

KQ 3 addresses the direct (head-to-head) evidence on comparative effectiveness of a psychological versus a pharmacological treatment.

KQ 4 synthesizes the evidence on adverse effects (AEs) associated with treatments of interest for adults with posttraumatic stress disorder (PTSD).

In addition, we examine whether either the efficacy or the comparative effectiveness of any studies included in KQ 1, 2, or 3 differs by patient characteristics or type of trauma exposure (KQs 1a, 2a, and 3a, respectively). We required studies described in these sections to compare efficacy or comparative effectiveness between one or more of the subgroups of interest, ideally via interaction analyses. Because of the substantial heterogeneity of the samples, interventions, and comparators of each included study, we did not conduct meta-analysis to obtain pooled estimates of subgroup differences across studies.

To answer this question, we present findings from included studies that reported outcomes for subgroups of interest (defined by patient or trauma factors) and compare the efficacy or comparative effectiveness across subgroups.

Findings discussed in this chapter come from studies rated as having low or medium risk of bias. Evidence tables in Appendix F provide additional information about the characteristics and findings from each study rated as having low or medium risk of bias. We excluded high risk of bias studies and this chapter does not include findings from these studies. Appendix G contains information about these high risk of bias studies that otherwise met all review inclusion criteria.

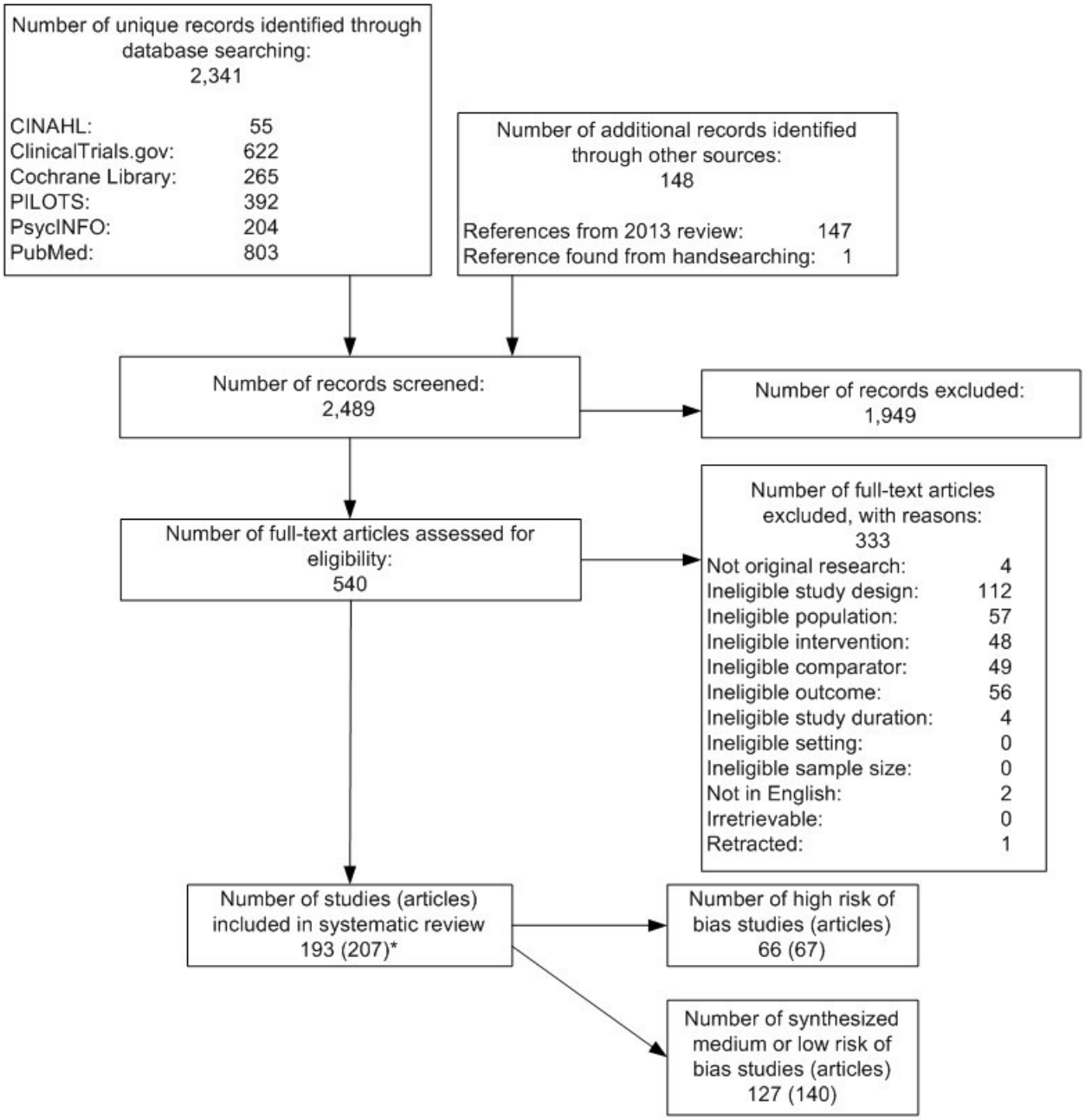
At the conclusion of this chapter, we include discussion of the evidence found in support of our two contextual questions.

Results of Literature Searches

Results of our searches appear in Figure 2. We included published articles reporting on 193 studies (207 articles). Of the included studies, all were randomized controlled trials (RCTs). We assessed the majority of included studies as medium risk of bias. We assessed eleven studies as

low risk of bias. Additional details describing the included studies are provided in the relevant sections of this results chapter.

Figure 2. Disposition of articles



* Of the 127 low or medium risk of bias studies published in 140 articles synthesized in this report, 39 studies (43 articles) are new evidence published since the prior review. Most of the new low or medium risk of bias evidence answers key question (KQ) 1 (34 studies in 38 articles), while a few answer KQ 2 (5 studies in 5 articles). Eight new low or medium risk of bias studies contribute to the evidence to answer KQ 4.

Table 4 describes common outcome measures used in this literature. For further details about these instruments and scales, see Appendix B. Definitive thresholds for clinically significant

changes are not well established for many of these measures, although some general guidelines exist (as noted in the table). For continuous outcomes for which a research team combined data from different scales measuring the same construct, a standardized mean difference (SMD) effect size of ~0.5 (a "medium" effect size)[118] or higher has been considered a threshold for clinically significant benefit.

Table 4. Outcome measure tools commonly used in the included trials

Abbreviated Name	Complete Name	Range of Scores
BDI[a]	Beck Depression Inventory	0 to 63
CAPS[b]	Clinician-Administered PTSD Scale	0 to 136
DGRP	Duke Global Rating for PTSD scale	1 = very much improved; 2 = much improved; >2 = nonresponders
DTS	Davidson Trauma Scale	0 to 136
GAF	Global Assessment of Functioning	0 to 100
HADS	Hospital Anxiety and Depression Scale	0 to 21
HAM-A or HAS	Hamilton Anxiety Rating Scale	0 to 56
HAM-D[a]	Hamilton Depression Rating Scale	0 to 54
IES	Impact of Event Scale	0 to 75
IES-R	Impact of Event Scale-Revised	0 to 88
MADRS	Montgomery-Åsberg Depression Rating Scale	0 to 60
MISS or M-PTSD	Mississippi Scale for Combat-related PTSD	35 to 175
PCL[c]	PTSD Checklist	17 to 85
PSS-I	PTSD Symptom Scale Interview	0 to 51
PSS-SR	PTSD Symptom Scale Self-report Version	0 to 51
PTDS or PDS	Posttraumatic Diagnostic Scale	0 to 51
Q-LES-Q-SF	Quality of Life Enjoyment and Life Satisfaction Short Form	0 to 70 (raw score)
SCL-90-R	Symptom Checklist- 90-Revised	0 to 360
SDS	Sheehan Disability Scale	0 to 30
SF-12	Medical Outcome Study Self-Report Form (12 item)	0 to 100
SF-36	36-Item Short Form Health Survey	0 to 100
SI-PTSD or SIP	Structured Interview for PTSD	0 to 68
SPRINT	Short PTSD Rating Interview	0 to 32
STAI	State–Trait Anxiety Inventory	20 to 80
WAS	Work and Social Adjustment Scale	0 to 40

[a] A 3-point improvement has been considered clinically meaningful.[119]
[b] Some experts suggest that a reduction of 15 points on the Clinician-Administered PTSD Scale (CAPS) constitutes a clinically significant reduction.[120]
[c] Some researchers have considered a reduction of 5 or more points to indicate a clinically significant response.[121]

KQ 1: Efficacy and Comparative Effectiveness of Different Psychological Treatments

We organized this section by type of psychological treatment and present the information in the following order: (1) cognitive behavioral therapy (CBT)-cognitive interventions; (2) CBT-coping skills; (3) CBT-exposure; (4) CBT-mixed therapies; (5) eye movement desensitization and reprocessing (EMDR); and (6) other psychotherapies, which include Seeking Safety (SS), imagery rehearsal therapy (IRT), interpersonal therapy (IPT), mindfulness-based stress reduction (MBSR), narrative exposure therapy (NET), brief eclectic psychotherapy (BEP), trauma affect regulation (TAR), memory specificity training (MEST), and emotional freedom techniques

(EFT). Table 5 presents the organization used to categorize the classes of psychological treatments identified by studies included in this review.

Table 5. Classes and categories of psychological treatments for posttraumatic stress disorder

Class of Treatment	Categories of Treatment	Subcategories of Treatment
Cognitive behavioral therapy (CBT)	CBT-cognitive interventions	Cognitive processing therapy (CPT) Cognitive restructuring (CR) Cognitive therapy (CT) Meta Cognitive Therapy (MCT)
	CBT-coping skills	Relaxation training Stress inoculation training (SIT) Structured approach therapy (SAT)
	CBT-exposure	Imaginal exposure (IE), In vivo exposure Prolonged exposure (PE) or modified PE (mPE) Concurrent Treatment of PTSD and Substance Use Disorders using Prolonged Exposure (COPE) Virtual reality exposure (VRE) Written exposure therapy (WET)
	CBT-M[a]	See footnote[a]
Eye movement desensitization and reprocessing (EMDR)	None	NA
Other psychotherapies	Brief eclectic psychotherapy (BEP)	NA
	Emotional freedom techniques (EFT)	NA
	Hypnosis	NA
	Interpersonal therapy (IPT)	NA
	Imagery rehearsal therapy (IRT)	NA
	Memory specificity training (MEST)	NA
	Mindfulness-based stress reduction (MBSR)	NA
	Narrative exposure therapy (NET)	NA
	Neurofeedback training (NF)	NA
	Seeking Safety (SS)	NA
	Trauma affect regulation (TAR)	NA

[a] Mixed CBT trials had elements of the following types: breathing retraining, cognitive restructuring, crisis/safety planning, exposure (imaginal, in vivo, or both), guided imagery, mindfulness training, psychoeducation, relapse prevention, relaxation training, self-monitoring, skills training, and stress management.

BEP = brief eclectic psychotherapy; CBT = cognitive behavioral therapy; CBT-M = CBT mixed; COPE = Concurrent Treatment of PTSD and Substance Use Disorders using Prolonged Exposure; CPT = cognitive processing therapy; CR = cognitive restructuring; CT = cognitive therapy; EFT = emotional freedom techniques; EMDR = eye movement desensitization and reprocessing; IE = imaginal exposure; IPT = interpersonal therapy; IRT = imagery rehearsal therapy; MBSR = mindfulness-based stress reduction; MEST = memory specificity training; mPE = modified PE; NA = not applicable; NET = narrative exposure therapy; NF = neurofeedback training; PCT = present-centered therapy; PDT = psychodynamic therapy; PE = prolonged exposure; SAT = structured approach therapy; SIT = stress inoculation training; SS = Seeking Safety; TAR = trauma affect regulation; VRE = virtual reality exposure; WRE = written exposure therapy.

The primary outcomes of interest that investigators used to determine the effectiveness of treatments for adults with PTSD include PTSD symptoms, loss of PTSD diagnosis, and symptom remission, as defined by study authors based on loss of symptoms below a predefined threshold level). We also comment on other outcomes of interest, such as prevention or reduction of coexisting medical or psychiatric conditions (especially depression, anxiety, and substance use problems), quality of life, and disability or functional impairment (to include returning to work or active duty status). The key points are based primarily on meta-analyses. When the lack of available evidence prevented pooling findings via meta-analysis, we relied on qualitative

synthesis of findings. Table 6 presents the summary of efficacy and strength of evidence (SOE) of PTSD psychological treatment studies included in this review.

Table 6. Summary of efficacy and strength of evidence of PTSD psychological treatments

Treatment	Outcome	N Trials (Subjects)	Findings	SOE
Cognitive processing therapy	PTSD symptoms[a]	5 (399)[1-4, 6]	Reduced PTSD symptoms SMD -1.35 (95% CI, -1.77 to -0.94)	Moderate
	Loss of PTSD diagnosis	4 (299)[1-4]	Greater loss of PTSD diagnosis RD 0.44 (95% CI, 0.26 to 0.62)	Moderate
	Depression symptoms[b]	5 (399)[1-6]	Reduced depression symptoms SMD -1.09 (95% CI, -1.52 to -0.65)	Moderate
Cognitive therapy	PTSD symptoms[a]	4 (283)[5, 7-9]	Reduced PTSD symptoms SMD of individual studies range from -2.0 to -0.3	Moderate
	Loss of PTSD diagnosis	4 (283)[5, 7-9]	Greater loss of PTSD diagnosis RD 0.55 (95% CI, 0.28 to 0.82)	Moderate
	Depression symptoms[b]	4 (283)[5, 7-9]	Reduced depression symptoms Between-group mean differences of individual trials ranged from -11.1 to -8.3	Moderate
Cognitive behavioral therapy-exposure	PTSD symptoms[a]	13 (885)[3, 10-21]	Reduced PTSD symptoms SMD -1.23 (95% CI, -1.50 to -0.97)	High
		8 (689)[3, 10, 11, 13, 16, 18, 20, 21]	SMD CAPS -1.12 (95% CI, -1.42 to -0.82)	
	Loss of PTSD diagnosis	6 (409)[3, 13, 14, 16, 17, 21]	Greater loss of PTSD diagnosis RD 0.56 (95% CI, 0.35 to 0.78)	High[c]

Treatment	Outcome	N Trials (Subjects)	Findings	SOE
Cognitive behavioral therapy-exposure (continued)	Depression symptoms[b]	10 (715)[3, 11-15, 18-21]	Reduced depression symptoms SMD -0.76 (95% CI, -0.91 to -0.60)	High
Cognitive behavioral therapy-mixed	PTSD symptoms[a]	 21 (1,349)[12, 14, 22-40] 11 (709)[22, 23, 27-29, 34-39]	Reduced PTSD symptoms SMD -1.01 (95% CI, -1.28 to -0.74) SMD -1.24 (95% CI, -1.67 to -0.81)	High[c]
	Loss of PTSD diagnosis	9 (474)[22-24, 31-34, 39, 41]	Greater loss of PTSD diagnosis RD 0.29 (95% CI, 0.11 to 0.41)	High[c]
	Depression symptoms[b]	15 (929)[12, 14, 22-24, 28, 29, 33, 35-40, 42]	Reduced depression symptoms SMD -0.87 (-1.14 to -0.61)	High[c]
Eye movement desensitization and reprocessing	PTSD symptoms[a]	8 (449)[13, 16, 43-48]	Reduced PTSD symptoms SMD -1.08 (95% CI, -1.82 to -0.35)	Moderate[d]
	Loss of PTSD diagnosis	7 (427)[13, 16, 43-45, 47, 48]	Greater loss of PTSD diagnosis RD 0.43 (95% CI, 0.25 to 0.61)	Moderate
	Depression symptoms[b]	7 (347)[13, 43-48]	Reduced depression symptoms SMD -0.91 (95% CI, -1.58 to -0.24)	Moderate
Brief eclectic psychotherapy	Loss of PTSD diagnosis	3 (96)[49-51]	Greater loss of PTSD diagnosis RD of individual studies ranged from 0.13 to 0.58	Low
	Depression symptoms[b]	3 (96)[49-51]	Reduced depression symptoms	Low
Imagery rehearsal therapy	PTSD symptoms[a]	1 (168)[52]	Reduced PTSD symptoms Between-group mean difference -21.0; p<0.05	Low

Treatment	Outcome	N Trials (Subjects)	Findings	SOE
Narrative exposure therapy	PTSD symptoms[a]	3 (232)[53-55]	Reduced PTSD symptoms SMD range from -1.95 to -0.79 across 3 individual studies	Moderate
	Loss of PTSD diagnosis	2 (198)[53, 54]	Greater loss of PTSD diagnosis RD of 0.06 and 0.43 in individual studies	Low
Seeking Safety	PTSD symptoms[a]	3 (232)[56-58]	Reduced PTSD symptoms SMD of individual trials ranged from -0.22 to 0.04	Low for no difference
Trauma affect regulation	PTSD symptoms[a]	2 (173)[59, 60]	Reduced PTSD symptoms Between-group mean difference of -17.4 and -2.7 in individual studies	Low

NOTE: Outcomes graded as insufficient are not included in this table.
[a] SMD from the Clinician-Administered PTSD Scale; SMD from various PTSD symptom scales.
[b] SMD from the Beck Depression Inventory; SMD from various depression symptom scales.
[c] SOE increased from moderate to high because of additional evidence of efficacy published since prior PTSD review.
[d] SOE increased from low to moderate because of additional evidence of efficacy published since prior PTSD review.

CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; N = number of subjects; PTSD = posttraumatic stress disorder; RD = risk difference; SMD = standardized mean difference; SOE = strength of evidence.

Within each section, we focus first on studies with inactive comparison groups (e.g., wait-list or usual care) to determine whether evidence supports the efficacy of each type of intervention. We then address studies with active comparison groups (i.e., head-to-head comparative evidence), or we provide cross-references for where those studies are addressed. In some cases, the active comparator was not an intervention for which we intended to assess the comparative effectiveness with an included treatment type (e.g., present-centered therapy [PCT] or patient education).

Tables describing characteristics of included studies are organized similarly. For most sections, we first provide details on studies that use any inactive comparators (in alphabetical order by last name of the first author) (i.e., those about efficacy) and then the details on any additional studies that included only active comparators.

In the bulleted text below, we summarize the main overall key points and then the key points for each type of psychotherapy. We also report grades for the SOE, where appropriate, which we determined after considering the evidence base of studies we had assessed as either low or medium risk of bias. For continuous outcomes such as PTSD, depression, and anxiety symptoms or ratings of quality of life or functioning, we present the between-group mean difference for single studies or the SMD when describing more than one study to indicate the between-group difference in pre- to posttreatment or pre- to followup assessments. For dichotomous outcomes like remission and loss of PTSD diagnosis, we report the risk difference (RD) between groups.

For outcomes with evidence from three or more studies with low heterogeneity across studies or five or more studies testing the same intervention types, we present the pooled estimate from

meta-analysis and the 95 percent confidence interval (CI). When we determined that three or four studies had substantial heterogeneity in sample, intervention, or study characteristics or two or fewer studies testing the same intervention presented data for an outcome, we qualitatively synthesized the findings and present findings from the individual studies.

All included studies are cited in the detailed synthesis section and related tables and figures presented for each treatment. Section headings within each detailed synthesis section include each outcome reported by at least one included study of that treatment type. If an outcome does not appear in the section, no included study testing the intervention of interest reported data on it.

Appendices contain additional information about the risk of bias assessments (Appendix E), individual study characteristics and findings for each outcome presented in evidence tables (Appendix F), characteristics and consistency of findings of high risk of bias studies not synthesized in the text (Appendix G), forest plots depicting individual and pooled study findings (Appendix H), and detailed information about each component contributing to the SOE grade (Appendix I).

Key Points: Overall—Efficacy of Psychological Treatments

- For PTSD symptoms reduction, CBT-exposure and CBT-mixed therapies provide high SOE of efficacy. Cognitive processing therapy (CPT), cognitive therapy (CT), EMDR, and NET provide moderate SOE of efficacy; TAR and IRT provide low evidence of efficacy.
- Low SOE supports no difference in efficacy of SS.
- For loss of PTSD diagnosis, CBT-exposure and CBT-mixed therapies provide high SOE of efficacy; CPT, CT, and EMDR provide moderate SOE of efficacy; NET and BEP provide low evidence of efficacy.
- Studies provide insufficient evidence of differences in efficacy by subgroups of interest defined by patient characteristics or type of trauma.

Key Points: Overall—Comparative Effectiveness of Psychological Treatments

- Few studies have tested comparative effectiveness of psychological interventions, precluding the use of meta-analysis to pool estimates.
- Moderate SOE favors CBT-exposure over relaxation for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms.
- Low SOE favors greater reduction in PTSD symptoms for CBT mixed (CBT-M) over relaxation therapy.
- Low SOE for no difference in effectiveness for reduction in PTSD symptoms for CBT-exposure versus EMDR and for reduction in depression symptoms for CBT-exposure versus CBT-exposure+cognitive restructuring (CR)

Key Points: CBT—Cognitive Interventions

- Moderate SOE supports the efficacy of CPT and CT for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms
- Moderate SOE supports the efficacy of CT for reduction in anxiety symptoms and reduction in disability.

Key Points: CBT—Coping Skills

- Insufficient evidence exists to determine the efficacy of relaxation, stress inoculation training (SIT), and structured approach therapy (SAT), with single studies testing each intervention.
- Moderate SOE supports the effectiveness of CBT-exposure compared with relaxation for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms
- Low SOE supports the effectiveness of CBT-mixed compared with relaxation for reduction in PTSD symptoms.

Key Points: CBT—Exposure

- High SOE supports the efficacy of CBT-exposure therapy for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms, and low SOE for anxiety symptoms.
- Moderate SOE provides comparative effectiveness of CBT-exposure compared with relaxation for reduction in PTSD symptoms and loss of PTSD diagnosis, and low SOE favors CBT-exposure over relaxation for reduction in depression symptoms.
- Low SOE shows no difference in effectiveness between CBT-exposure and EMDR for reduction in PTSD symptoms and between CBT-exposure and CBT-exposure+CR for reduction in depression symptoms.

Key Points: CBT—Mixed

- High SOE supports the efficacy of CBT-mixed for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms.
- Moderate SOE supports the efficacy of CBT-mixed for reduction in anxiety symptoms and reduction in substance use issues.
- Low SOE supports the efficacy of CBT-mixed for reduction in disability/functional impairment.
- Low SOE supports the comparative effectiveness of CBT-mixed over relaxation for reduction in PTSD symptoms.

Key Points: EMDR

- Moderate SOE supports the efficacy of EMDR for reduction in PTSD symptoms, loss of diagnosis, and reduction in depressive symptoms.
- Low SOE shows no difference in effectiveness for reduction in PTSD symptoms between EMDR and CBT-exposure.

Key Points: Other Psychological Interventions

- Low SOE supports the efficacy of TAR for reduction in PTSD symptoms.
- Low SOE supports the efficacy of BEP for loss of PTSD diagnosis, reduction in depression symptoms, and reduction in anxiety symptoms.
- Low SOE supports efficacy of IRT for reduction in PTSD symptoms.
- Moderate SOE supports the efficacy of NET for reduction in PTSD symptoms and low SOE supports its efficacy for loss of PTSD diagnosis. Low SOE supports no difference of SS versus inactive comparator on reduction in PTSD symptoms.

Detailed Synthesis: CBT—Cognitive Interventions

Characteristics of Studies

Table 7 summarizes the characteristics of the 14 cognitive intervention studies that met our inclusion criteria. We divided the 14 cognitive interventions further into CPT (7 studies), CR (1 study), CT (5 studies), and meta cognitive therapy (MCT) (1 study).

Table 7. Characteristics of included cognitive intervention trials

Study	Arm (N)	Duration of Treatment (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	Percent Female	Percent Non-white	Risk of Bias
Chard et al., 2005[2]	CPT (36) MA (35)	17 weeks (3 and 12 months)	Female Childhood sexual abuse	65.5 to 68.3	33	100	19	Medium
Ehlers et al., 2003[5]	CT (28) SHB (28) RA (29)	Mean of 9 weeks, 0 to 3 booster sessions (3, 6, and 9 months)	Male and female MVA	PDS (frequency) 30.0 PDS (distress) 30.8	39	72	97	Medium
Ehlers et al., 2005[8]	CT (14) WL (14)	4 to 12 weeks plus up to 3 monthly boosters (3 and 6 months)	Male and female Mixed	CAPS (frequency) 31.6 to 42.0 CAPS (intensity) 29.0 to 36.5	37	54	4	Medium
Ehlers et al., 2014[9]	Intensive CT (30) Standard CT (31) Supportive Therapy (30) WL (30)	14 weeks (27 weeks, 40 weeks for all but WL)	Chronic PTSD Mixed	73	39	59	30	Low
Forbes et al., 2012[4]	CPT (30) TAU (29)	12 weeks (3 months)	Male and female Military related	65.8 to 75.5	53	3	0	Medium

Study	Arm (N)	Duration of Treatment (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	Percent Female	Percent Non-white	Risk of Bias
Galovski et al., 2012[6]	Modified CPT (53) Symptom-monitoring delayed treatment (47)	4–18 sessions for Modified CPT arm; 10 weeks for WL arm (followup data gathered after cross-over not reported).	Physical/sexual assault (as a child or an adult)	74 to 77	40	69	58	Medium
Marks et al., 1998[122] Lovell, et al., 2001[123]	PE (23) CR (13) CR+PE (24) Relax (21)	10 sessions[b] (mean of 16 weeks), (1, 3, and 6 months)	Male and female Mixed	NR	38	36	NR	Medium
Maxwell et al., 2016[124]	MEST (8) CPT (8)	6 weeks (post, 3 months)	Male and female Mixed	MPSS-SR 54.13 to 63.50	NR	81	44	Medium
Monson et al., 2006[1]	CPT (30) WL (30)	10 weeks (1 month)	Male and female Combat	76.7 to 79.1	54	10	4	Medium
Mueser et al., 2008[7]	CT (54) UC (54)	12 to 16 sessions (post)[b]	Male and female Mixed	74.5 to 76.2	44	79	16	Medium
Resick et al., 2002[3] Resick, et al., 2003[125] Resick, et al., 2012[126]	CPT (62) PE (62) MA (47)	6 weeks (3 and 9 months, 5 to 10 years)	Female Sexual assault	69.9 to 76.6	32	100	29	Medium
Resick et al., 2015[127, 128]	Group CPT-C (56) Group PCT (52)	6 weeks (2 weeks post-tx, 6 months after start of treatment, 12 months after start of treatment)	Military trauma (although could also have had PTSD attributed to other previous trauma)	PCL-S 58 to 59	32	7	43	Medium
Tarrier et al., 1999[129, 130]	IE (35) CT (37)	16 sessions (112 days) (6 and 12 months)	Male and female Mixed	71.1 to 77.8	39	42	NR	Medium
Wells et al., 2014[19]	MCT (11) PE (11) WL (10)	8 weekly sessions (post)	Mixed	PDS 33 to 38	41	38	NR	Medium

[a] Data reported are mean CAPS total or range of mean CAPS total scores across groups unless otherwise specified.
[b] Number of treatment sessions is reported when duration of treatment was not specified.

CAPS = Clinician-Administered PTSD Scale; CPT = cognitive processing therapy; CT = cognitive therapy; CR = cognitive restructuring; IE = imaginal exposure; MA = minimal attention (a type of wait-list group); MCT = meta cognitive therapy; MEST = memory specificity training; MPSS-SR = Modified PTSD Symptom Scale-Self-Report; MVA = motor vehicle accident; N = total number randomized/assigned to intervention and control groups; NR = not reported; PCT = present-centered therapy; PDS = Posttraumatic Diagnostic Scale; PE = prolonged exposure; PTSD = posttraumatic stress disorder; RA = repeated assessments (a type of wait-list group); SHB = self-help booklet based on principles of CBT; TAU = treatment as usual; UC = usual care; WL = wait-list; y = year.

Of the seven CPT interventions, four had wait-list comparators,[1-3, 6] one had a usual-care comparator,[4] and three had active intervention comparators (prolonged exposure [PE],[3] MEST,[124] and group PCT).[127] The single CR study had three active comparators: relaxation, PE, and a combined CR and PE.[122] Five studies tested CT: three had wait-list comparators,[5, 8, 9] one had a usual care comparator,[7] and two had active comparators[9] (self-help booklet[5] and imaginal exposure[129]). The single MCT study had one active comparator, PE, and one inactive comparator, wait-list.[19] Further details describing the included studies are provided in Appendix F.

Of the seven CPT studies, sample sizes ranged from 16 to 171. Duration of treatment ranged from 6 to 17 weeks. Five studies included at least one posttreatment followup assessment after 1 to 12 months,[1-4, 124] one study reported followup data but had a cross-over design affecting time period comparisons across groups,[6] and one study reported outcomes at 5 to 10 years followup.[126] Three studies enrolled all or a majority of females with sexual abuse or assault trauma types,[2, 3, 6] and three studies enrolled all or a majority of males with combat-related trauma types.[1, 4, 127] The mean age of participants in the CPT studies ranged from 32 to 54 years. The primary outcome measures for these studies were the Clinician-Administered PTSD Scale (CAPS), PTSD Checklist (PCL), Modified PTSD Symptom Scale (MPSS), and PTSD Symptom Scale (PSS).

The single CR study that contained three active comparators included males and females with exposure to mixed trauma types.[122] Participants completed 10 sessions over a mean of 16 weeks and had followup assessments at 1, 3, and 5 months posttreatment. The primary outcome measure was the Impact of Event Scale (IES).

Of the five CT studies, sample sizes ranged from 28 to 121. Duration of treatment ranged from about 3 to 5 months. Although one study did not include a followup assessment after posttreatment,[7] the other four studies included at least one followup period 6 to 12 months posttreatment. All four studies with inactive comparators enrolled a majority of female participants;[5, 7-9] two of these also had active comparator arms.[5, 9] The single study that compared CT with imaginal exposure (IE)[129] had similar proportions of male and female participants. One study included those with motor vehicle accident (MVA) trauma types;[5] the other study participants had mixed types of trauma exposures. The mean age of participants in CT studies ranged from 37 to 44. All studies used the CAPS as the primary outcome of interest.

The single MCT study that had one active comparator (PE) and one inactive comparator (wait-list) included males and females with exposure to mixed trauma types. The single CR study that contained three active comparators included males and females with exposure to mixed trauma types.[122] Participants completed eight sessions and did not include any followup assessments after the end of treatment. The primary outcome measure was the Posttraumatic Diagnostic Scale (PDS).

Results for Cognitive Interventions Compared With Inactive Comparators

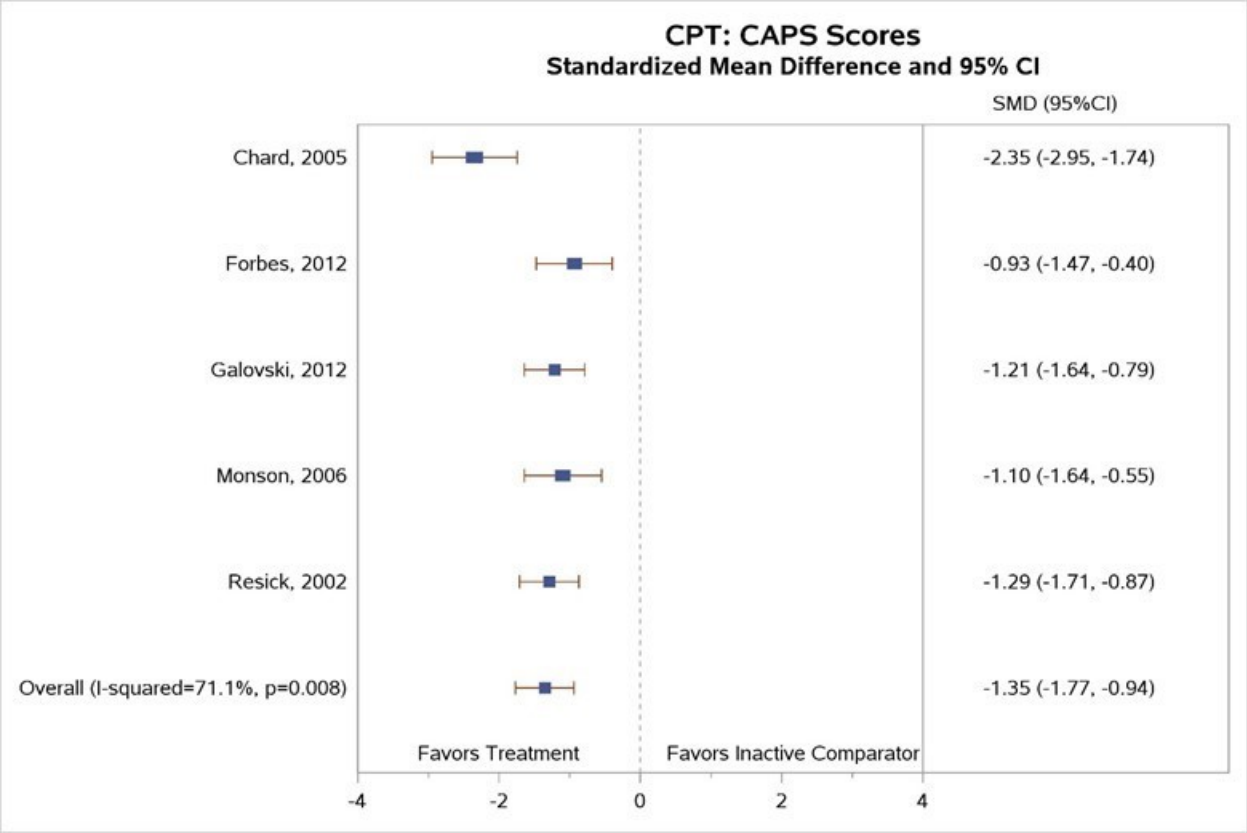
Under each outcome heading below, we first present our data synthesis for studies testing CPT against an inactive comparator. Then we present results for the CR study, CT studies, and MCT study with inactive comparator groups.

PTSD Symptoms

All included studies reported measures of PTSD symptoms. All five studies comparing CPT with inactive comparators found that subjects in the CPT arm had a greater reduction in CAPS-assessed symptoms of PTSD than those in the inactive comparator arm.[1-4, 6] The meta-analysis that pooled CAPS scores (Figure 3) found a much greater decrease in PTSD symptoms for subjects treated with CPT therapy than for those in inactive comparator groups (SMD, -1.35; 95% CI, -1.77 to -0.94, I^2=71.1%, 5 studies, N=399, moderate SOE). The meta-analysis had considerable statistical heterogeneity, but the direction of effects was consistent. The differences were only in the exact magnitude of benefit; all studies found moderate or large magnitudes of benefit. In addition, two of three studies that compared CPT with a wait-list group found that changes were maintained at 3 to 6 months (posttreatment) followup.[2, 3]

All four studies that compared CT with inactive control groups reported significantly greater decreases in PTSD symptoms for those treated with CT than those in inactive comparator groups (meta-analysis not performed because of heterogeneity in sample and study characteristics, SMD of individual studies ranged from -2.0 to -0.3; 4 studies; N=236; moderate SOE).[5, 7-9] The single study that compared MCT with an inactive comparator reported significantly greater decreases in PDS-measured PTSD symptoms, favoring MCT, as measured by the PDS (between-group mean difference=-27.7, 1 study, N=21; insufficient SOE).[19]

Figure 3. Standardized mean change in PTSD symptoms (measured by the Clinician-Administered PTSD Scale) for CPT compared with inactive comparators

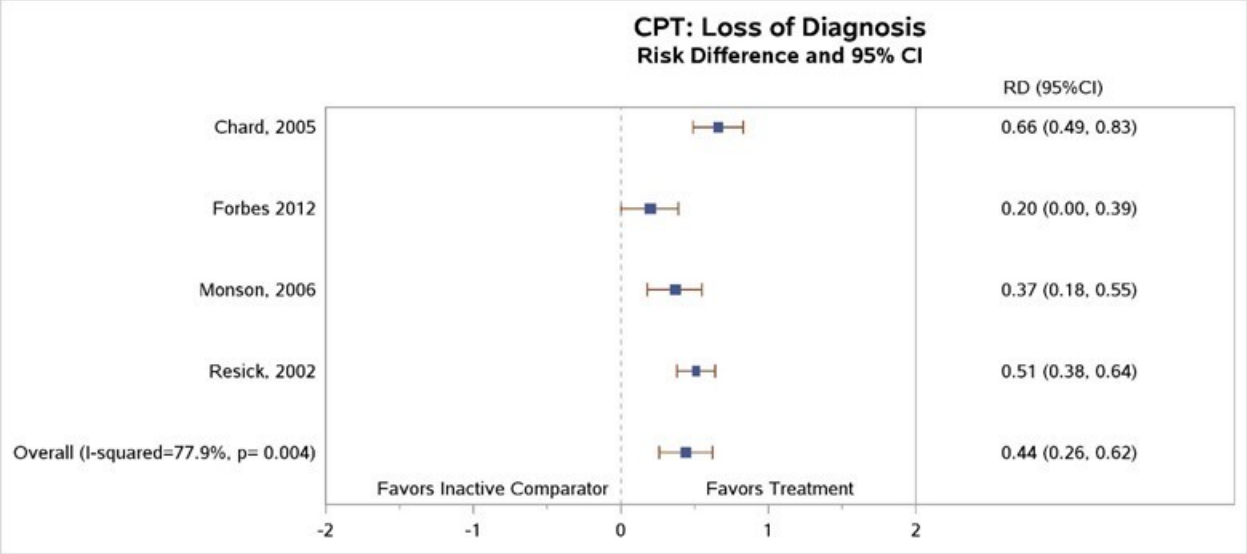


CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; CPT = cognitive processing therapy; PTSD = posttraumatic stress disorder; SMD = standardized mean difference.

Loss of PTSD Diagnosis

Several cognitive intervention studies reported data on posttreatment diagnostic status. The four CPT studies that reported loss of diagnosis outcomes favored CPT over inactive comparator (risk difference [RD], 0.44; 95% confidence interval [CI], 0.26 to 0.62; I^2, 77.9%; 4 studies, N=299; moderate SOE)[1-4] (Figure 4). All four studies comparing CPT with wait-list reported followup assessments showing that, over time, the greater changes seen in loss of PTSD diagnosis among CPT participants than inactive comparator participants persisted at 1 month,[1] 12 months,[2, 3] and 5 to 10 years after the end of treatment.[126]

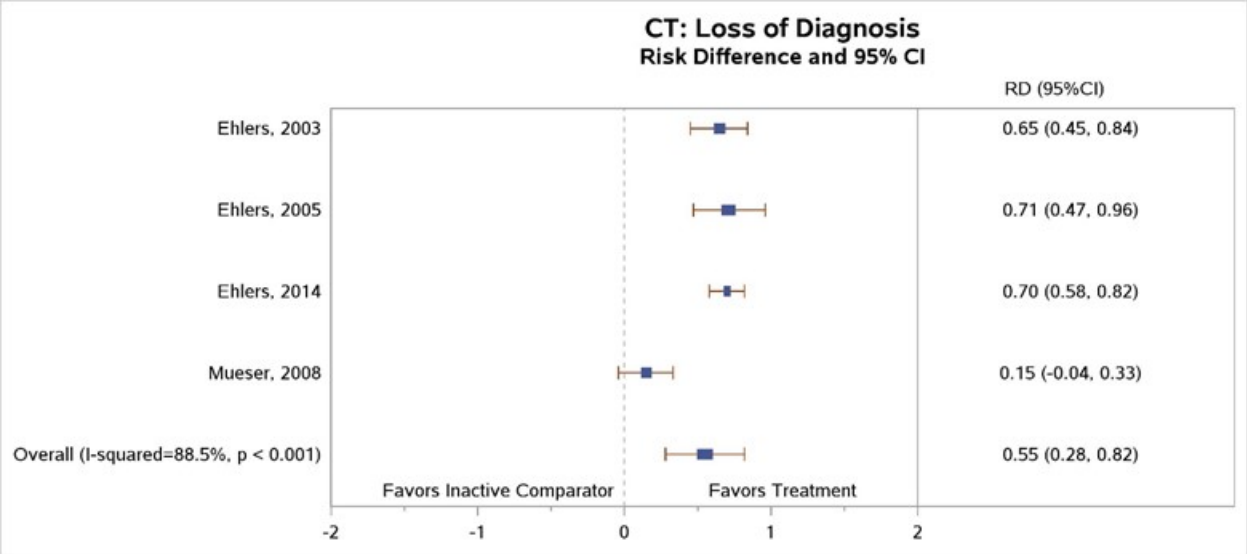
Figure 4. Loss of diagnosis for CPT compared with inactive comparators



CI = confidence interval; CPT = cognitive processing therapy; RD = risk difference.

Three[5, 8, 9] of the four studies[5, 7-9] that compared loss of PTSD diagnosis between CT and inactive comparators found significantly higher rates of loss of PTSD diagnosis at posttreatment among those who received the CT intervention as compared with those who received an inactive comparator (RD, 0.55; 95% CI, 0.28 to 0.82; I^2, 88.5%; 4 studies, N=314; moderate SOE) (Figure 5).

Figure 5. Loss of diagnosis for CT compared with inactive comparators



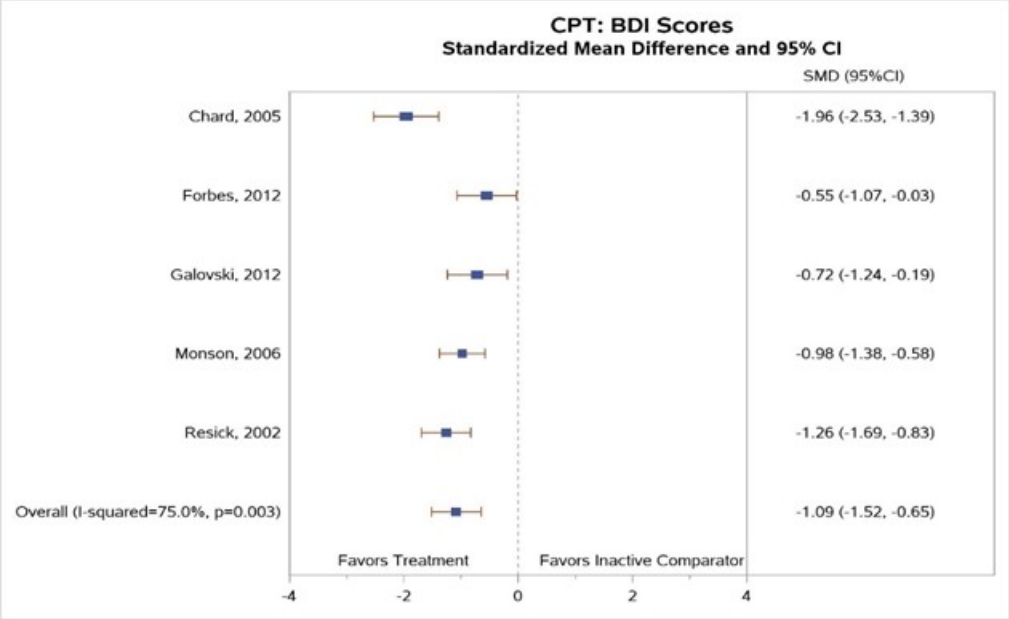
CI = confidence interval; CT = cognitive therapy; RD = risk difference.

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

All but one[127] cognitive intervention study assessed coexisting depressive symptoms using the Beck Depression Inventory (BDI) or BDI-II, and some also assessed anxiety symptoms.[1-6] Our meta-analysis of the five CPT studies reporting BDI or BDI-II scores (Figure 6) found greater improvement in depression symptoms for subjects treated with CPT than for those in

inactive comparison groups (SMD, -1.09; 95% CI, -1.52 to -0.65, I^2=75.0, 5 studies, N=399, moderate SOE).[1-4, 6]

Figure 6. Standardized mean change in depressive symptoms (measured by the Beck Depression Inventory) for CPT compared with inactive controls



BDI = Beck Depression Inventory; CI = confidence interval; CPT = cognitive processing therapy; SMD = standardized mean difference.

In three studies that included followup assessments of depressive symptoms, subjects maintained significant decreases in symptoms at 3 months[3-5] and 9 months[3] after the end of treatment assessment. In another study, authors found a pre- to posttreatment depressive symptom effect size of 1.16 for CPT versus inactive comparator group, which declined to 0.49 at the 1-month followup.[1] The authors attributed the attenuation of between-group effect size differences to decreases in depressive scores in the wait-list group at followup, not to increases in depressive symptom scores in the CPT group. From the above findings and our meta-analysis, we concluded that evidence supports the efficacy of CPT for reducing depression symptoms (moderate SOE).

Two studies of CPT assessed anxiety symptoms as an outcome using the State-Trait Anxiety Inventory (STAI).[1, 4] One found CPT to be no more effective in reducing symptoms of anxiety than wait-list;[1] the other found greater improvement in anxiety for subjects treated with CPT than those receiving usual treatment from intake to posttreatment (p=0.018).[4, 5] We concluded insufficient evidence to determine the efficacy of CPT for reducing anxiety symptoms based on lack of consistency and imprecise findings of two studies.

All four studies that compared CT with inactive control groups assessed depressive and anxiety symptoms;[5, 7-9] four of four studies found significant between-group differences in depression symptoms and three of four studies found significant between-group differences at posttreatment favoring the CT group (moderate SOE). In two of the studies, between-group differences favoring the CT group persisted at the 3- and 9-month followup assessments (p<0.001 for all comparisons).[5, 7, 9]

The single MCT study reported significantly greater decreases in both depressive symptoms assessed with the BDI and anxiety symptoms assessed with the Beck Anxiety Inventory (BAI) among MCT group participants than inactive comparator participants (insufficient SOE).[19]

Quality of Life

Two studies compared quality-of-life outcomes between CPT and inactive comparator groups.[4, 6] One study[4] reported significant time by condition interactions for social quality-of-life measures but not for physical quality-of-life measures.[4] The other study found that CPT participants had significantly greater changes in quality-of-life ratings at posttreatment than those in the inactive comparator group (insufficient SOE).[6]

Two studies compared CT and inactive comparator groups on quality-of-life outcomes. One study of adults with PTSD and serious mental illness found that the CT group subjects had[7] better quality-of-life outcomes than the usual-care group for the physical quality-of-life measures ($p=0.002$) but not for mental quality-of-life measures ($p=0.13$). The other CT study with quality-of-life outcomes reported significant improvements among those enrolled in the CT groups as compared with the inactive comparator groups (insufficient SOE).[9]

Disability or Functional Impairment

Three studies that compared CT to an inactive comparator assessed disability using the Sheehan Disability Scale.[5, 8, 9] All studies reported significant improvements in disability among CT group participants as compared with inactive control participants at posttreatment and followup assessments (moderate SOE).

Results for Cognitive Interventions Compared With Active Comparators

Two studies tested cognitive interventions with a comparator for which we did not aim to assess comparative effectiveness (CPT versus PCT[9, 127] and CT versus self-help booklet[5]).

Two studies compared CPT with exposure therapy,[3, 122] one study compared CT with IE,[129, 130] and one study compared MCT with PE.[19] Assessment of these comparative effectiveness studies appears in the CBT-Exposure section below.

One study compared CPT with MEST.[124] Comparative effectiveness findings appear in the Other Psychological Interventions section below.

One study compared CR with a relaxation group and a combination of PE and CR.[122] The CR versus relaxation comparisons appear in the CBT-Coping Skills section (below). The authors did not report data on the comparative effectiveness of CR and the combination of PE and CR.

Detailed Synthesis: CBT—Coping Skills

Characteristics of Studies

Table 8 summarizes the characteristics of the six studies meeting our inclusion criteria.[14, 46, 122, 131-133] Further details describing the included studies are provided in Appendix F.

The studies in this section had a "coping skills" arm(s)—either relaxation training, SIT, or SAT. SIT is a cognitive behavioral intervention for PTSD in which the basic goal is to help subjects gain confidence in their ability to cope with anxiety and fear stemming from trauma-related reminders. In SIT, the therapist helps patients increase their awareness of trauma-related cues for fear and anxiety. In addition, clients learn a variety of coping skills that are useful in

managing anxiety, such as muscle relaxing and deep breathing. SAT contains components of SIT to include psychoeducation, skills training, and an application phase to practice new coping skills.

Table 8. Characteristics of included coping skills trials

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Carlson et al., 1998[46]	Relax (13) EMDR (10) TAU (12)	6 weeks (3 and 9 months)	Male Vietnam combat veterans	M-PTSD 117.5 to 119.4	48.5	0	45.7	Medium
Foa et al., 1999[14] Zoellner et al., 1999[134]	SIT (26) PE (25) PE+SIT (30) WL (15)	9 weeks (3, 6, and 9 months)	Female Assault	PSS-I 29.4 to 32.9	35	100	36	Medium
Markowitz et al., 2015[132] Markowitz et al., 2016[135]	PE (38) IPT (40) Relax (32)	14 weeks (post)	Chronic PTSD Mixed	68.9 to 72.1	40	77	35	Medium
Marks et al., 1998[122] Lovell, et al., 2001[123]	Relax (21) PE (23) CR (13) CR+PE (24)	10 sessions[b] (mean of 16 weeks) (1, 3, and 6 months)	Male and female Mixed	NR	38	36	NR	Medium
Sautter et al., 2015[131]	SAT (29) PFE (28)	12 sessions (post, 12 weeks)	U.S. combat veterans	83 to 86	33	2	6,334	Medium
Taylor et al., 2003[133]	Relax (19) PE (22) EMDR (19)	8 weeks (1 and 3 months)	Male and female Mixed	NR	37	75	23	Medium

[a]Data reported are mean CAPS or range of mean CAPS scores across groups unless otherwise specified.
[b]Number of treatment sessions is reported when duration of treatment was not specified.

CPT = cognitive processing therapy; CR = cognitive restructuring; EMDR = eye movement desensitization and reprocessing; F = female; IPT = interpersonal therapy; M-PTSD = Mississippi Scale for Combat-related PTSD; N = total number randomized/assigned to intervention and control groups; NR = not reported; PE = prolonged exposure; PFE = PTSD Family Education; PSS-I = PTSD Symptom Scale—Interview; PTSD = posttraumatic stress disorder; relax = relaxation; SAT=structured approach therapy; SIT = stress inoculation training; TAU = treatment as usual; WL = wait-list; y = year.

Two of the six studies compared coping skills interventions with inactive comparators.[14, 46, 122, 131-133] One compared PE, SIT, combined PE+SIT, and a wait-list group,[14] and the other compared relaxation, EMDR, and usual care.[46] One enrolled women who were victims of sexual or nonsexual assault,[14] and the other study enrolled combat veterans with mixed trauma types.[46] Duration of treatment ranged from 6 to 9 weeks, and both had multiple followup assessments up to 9 months after the end of treatment. The primary outcome measure for one study was the PSS-I;[14] and the other used the CAPS as the primary outcome measure.[46]

All six studies made comparisons with active psychotherapy interventions. Sample sizes ranged from 35 to 110. Duration of treatment ranged from 6 to 16 weeks. All but one study[132] included at least one followup assessment. Two studies enrolled combat veterans;[46, 131, 136] one enrolled victims of sexual and nonsexual assault;[14] and the other three studies enrolled heterogeneous groups of subjects with a variety of index trauma types (e.g., physical assault, road accidents, nonroad accident, witnessing a trauma or homicide, sexual assault, being held hostage, bombing, combat). Mean age for subjects in the studies ranged from 35 to 48.5. Whereas three studies had over 75 percent female participants,[14, 132, 133] two studies had samples

comprising at least 75 percent males.[46, 131] The primary outcome for nearly all studies was the CAPS; one study used the PSS-I.[14]

Results for Coping Skills Compared With Inactive Comparators

PTSD Symptoms

Both studies that compared a coping skills intervention with inactive comparators reported measures of PTSD symptoms (Table 9).[14, 46] One small study found significantly greater decreases in PTSD symptoms at posttreatment among participants in the SIT versus wait-list group.[14] The other study found a greater, but nonstatistically significant reduction in PTSD symptoms in the relaxation arm as compared with the treatment-as-usual arm (insufficient SOE).[46]

Table 9. Results of the coping skills interventions compared with inactive controls for PTSD

Study	Arm (N)	Outcome Measure(s)	Between Group Pre-Post Treatment Mean Difference	P-Value
Carlson et al., 1998[46]	Relax (13) TAU (12)	M-PTSD	-0.2	NS
		PTSD symptoms[a]	-0.8	NR
		IES-Total	5.7	NS
Foa, 1999 et al.,[14] Zoellner, 1999[134]	SIT (26) WL (15)	PSS-I	-10.5	<0.05

[a]This was a global self-rating on a 0 to 10 scale with 10 = "worst."

Note: Results are only presented for the relevant arms for this section (coping skills and inactive comparators).

IES = Impact of Event Scale; M-PTSD = Mississippi Scale for Combat-related PTSD; N = total number randomized to intervention and control groups; NR = not reported; NS = not significant; PSS-I = Posttraumatic Stress Disorder Symptom Scale-Interview; PTSD = posttraumatic stress disorder; relax = relaxation; SIT = stress inoculation training; TAU = treatment as usual; WL = wait-list.

Loss of PTSD Diagnosis

One small study reported loss of diagnosis data across treatment groups; comparisons favored SIT (RD, 0.42, $p<0.001$; insufficient SOE).[14]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Two studies reported on coexisting comorbid depression symptoms and comorbid anxiety symptoms (Table 10).[14, 46] The study that included SIT and wait-list arms found that subjects treated with SIT had greater decreases in depression symptoms than those in the wait-list group; between-group differences in pre- to posttreatment changes in anxiety symptoms did not reach statistical significance (insufficient SOE).[14]

The study comparing relaxation and usual care found decreases in both depression and anxiety symptoms in the relaxation group; however, the authors reported no statistically significant between-group difference on measures of anxiety and did not provide data on between-group differences for depression (insufficient SOE).[46]

Table 10. Results at the end of treatment for depression and anxiety symptoms for coping skills interventions compared with inactive controls

Study	Arm (N)	Outcome Measure(s)	Between Group Pre-Post Treatment Mean Difference	P-Value
Carlson et al., 1998[46]	Relax (13) TAU (12)	BDI	-7.3	NR
		STAI-State subscale	-5.3	NS
		STAI-Trait subscale	-1.3	NS
Foa et al., 1999[14]	SIT (26)	BDI	-8.5	<0.05
Zoellner et al., 1999[134]	WL (15)	STAI-State subscale	-11.4	NS

Note: Results are only presented for the relevant arms for this section (coping skills and inactive comparators).

BDI = Beck Depression Inventory; N = total number randomized to treatment and control groups; NR = not reported; NS = not statistically significant at p<0.05; relax = relaxation; SIT = stress inoculation training; STAI = State-Trait Anxiety Inventory; TAU = treatment as usual; WL = wait-list.

Results for Coping Skills Compared With Active Comparators

Of the six studies comparing a coping skills therapy with an active comparator, four included comparisons with exposure-based interventions,[14, 122, 132, 133] two included comparisons with EMDR,[46, 133] two included comparisons with CBT-mixed therapies,[14, 122] one included a comparison with CR,[122] one included a comparison with IPT,[132] and one compared to an active control condition for which we did not aim to assess comparative effectiveness (PTSD family education [PFE]).[131] For assessment of the comparisons with exposure-based therapies, see the CBT—Exposure section (below). For assessment of the comparisons with CBT-mixed therapies, see the CBT—Mixed section (below). For assessment of the comparisons with EMDR, see the EMDR section (below). For assessment of the comparisons with IPT, see the Other Psychological Interventions section (below).

Results for Coping Skills Compared With Active Comparators: Relaxation Training Versus Cognitive Restructuring

One study assessed the comparative effectiveness of four PTSD treatments; subjects in one arm received relaxation training and subjects in another arm received CR (the other two treatment arms tested CBT-exposure interventions; the CBT-exposure section details the findings from these comparisons).[122]

PTSD Symptoms

The study that enabled comparisons between relaxation training and CR found no significant between-group differences in the percentage of subjects who experienced a 50 percent pre- to posttreatment decrease in PTSD symptoms as assessed by the PSS (insufficient SOE).[122]

Loss of PTSD Diagnosis

More subjects in the CR group experienced a loss of PTSD diagnosis than those in the relaxation training group; the difference was not statistically significant (RD=-0.05 favoring CR, p=ns; insufficient SOE).[122]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

CR group subjects had greater depressive symptoms decreases than relaxation training group subjects, but not significantly so (RD=0.10, p=ns; insufficient SOE).[122]

Detailed Synthesis: CBT—Exposure

Characteristics of Studies

Table 11 summarizes the characteristics of the 25 studies meeting our inclusion criteria. Types of exposure therapy tested included IE, in vivo exposure, PE (which includes both components of IE and in vivo exposure, or modified PE, mPE), virtual reality exposure (VRE), written exposure therapy (WRE), and Concurrent Treatment of PTSD and Substance Use Disorders using Prolonged Exposure (COPE). Further details are provided in Appendix F. Of the 25 included studies, 14 studies (15 articles because one study reported similar outcomes across two separate publications) compared exposure therapy with an inactive comparator: wait-list,[3, 11-14, 16-19, 21, 122, 137] or usual care,[10, 15, 20, 41, 138, 139] and 17 included one or more active comparators.[3, 12-14, 16, 19, 41, 42, 122, 129, 132, 133, 138-140]

Table 11. Characteristics of included CBT-exposure trials

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Asukai et al., 2010[10]	PE (12) UC (12)	8 to 15 weekly sessions (3 and 12 months)	Male and female Mixed	84.3 to 84.6	29	88	100	Medium
Basoglu et al., 2007[11]	In vivo (16) WL (15)	1 session[b] (4, 8, 12, 24 weeks and 12 months)	Male and female Natural disaster	62.3 to 63.1	34	87	NR	Medium
Bryant et al., 2003[41]	IE (20) IE+CR (20) SC (18)	8 weeks	Male and female Mixed	CAPS-I intensity 32.5 to 32.9	35	52	NR	Medium
Bryant et al., 2008[42]	PE (31) PE+CR (28) IE (31) In vivo (28)	8 weeks	Male and female Mixed	71.4 to 76.8	37	NR	8	Medium
Coffey et al., 2016[140]	mPE+MET-PTSD (40) mPE (45) HLS (41)	9 to 12 sessions (post, 3 months, 6 months)	Mixed, combat related trauma excluded	76 to 82	34	46	21	Medium
Foa et al., 1999[14] Zoellner et al., 1999[134]	PE (25) SIT (26) PE+SIT (30) WL (15)	9 weeks (3, 6, and 9 months)	Female Assault	PSS-I 29.4 to 32.9	35	100	36	Medium
Foa et al., 2005[12]	Total 190 PE (NR) PE+CR (NR) WL (NR)	12 weeks; 9 to 12 weekly sessions (3, 6, and 12 months)	Female Assault	PSS-I 31.1 to 34.0	31	100	51	Medium
Fonzo et al., 2017[137] Fonzo et al., 2017[21]	PE (36) WL (30)	9 to 12 weekly or biweekly sessions	Male and female Mixed	66 to 71	36	65	NR	Medium

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Gamito et al., 2010[141]	VRE (5) IE (2) WL (3)	12 sessions[b]	Male Combat	NR	64	0	NR	Medium
Langkaas et al., 2017[142]	PE (31) IRT (34)	10 weeks (post, 12 months)	Male and female Mixed	PSS-I 33.2 to 34.9	45	58	NR	Medium
Markowitz et al., 2015[132] Markowitz et al., 2016[135]	PE (38) IPT (40) Relax (32)	14 weeks	Chronic PTSD	68.9 to 72.1	40	77	35	Medium
Marks et al., 1998[122] Lovell et al., 2001[123]	PE (23) CR (19) PE+CR (24) Relax (21)	10 sessions,[b] mean of 16 weeks (1, 3, and 6 months)	Male and female Mixed	CAPS Severity 2.6 to 3.2	38	36	NR	Medium
Mills et al., 2012[20]	COPE+TAU (55) TAU (48)	13 sessions (post)	Mixed	89 to 91	34	62	NR	Medium
Nacasch et al., 2011[15]	PE (15) TAU (15)	9 to 15 weeks (12 months)	Male and female Combat	PSS-I 36.8 to 37.1	34	NR	100	Medium
Reger et al., 2016[18]	VRE (54) PE (54) WL (54)	10 sessions (post, 3 months, 6 months)	Activity duty military	78 to 80	30	4	40	Medium
Resick et al., 2002[3] Resick, et al., 2003[125] Resick, et al., 2012[126]	PE (62) CPT (62) WL (47)	6 weeks (3 and 9 months, 5 to 10 years)	Female Sexual assault	69.9 to 76.6	32	100	29	Medium
Rothbaum et al., 2005[13]	PE (24) EMDR (26) WL (24)	4.5 weeks (6 months)	Female Sexual assault	Data reported in graphs only	34	100	32	Medium
Ruglass et al., 2017 [143]	COPE (39) Relapse Prevention (43) AMCG (28)	12 weeks (post, 1, 2, and 3 months)	Male and female Mixed 65% with clinical PTSD	46.39 to 57.70	44	36	82	Medium
Schnurr et al., 2003[139]	Group exposure (180) PCT (180)	30 weeks, 5 subsequent monthly boosters (12 months total)	Male Combat	80.4 to 82.1	51	0	34	Low
Schnurr et al., 2007[138]	PE (141) PCT (143)	10 weeks (3 and 6 months)	Female Mixed	77.6 to 77.9	45	100	46	Medium
Sloan et al., 2012[17]	WET (22) WL (24)	10 sessions for WET group/5 weeks for WL group (post, 18 weeks)	MVA	NR	41	65	63	Low
Tarrier et al., 1999[129, 130]	IE (35) CT (37)	16 sessions (16 weeks) (6 and 12 months)	Male and female Mixed	71.1 to 77.8	39	42	NR	Medium

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Taylor et al., 2003[133]	PE (22) EMDR (19) Relax (19)	6 months	Male and female Mixed	NR	37	75	23	Medium
van den Berg et al., 2015[16]	PE (53) EMDR (55) WL (47)	8 weeks (post, 6 months)	Psychotic disorders and PTSD Mixed	70	41	54	NR	Low
Wells et al., 2014[19]	MCT (11) PE (11) WL (10)	8 sessions (post)	Mixed	PDS 33 to 38	41	38	NR	Medium

[a] Data reported are mean CAPS or range of mean CAPS scores across groups unless another instrument is specified.
[b] Number of treatment sessions is reported when duration of treatment was not specified

AMCG = active monitoring control group; CAPS = Clinician-Administered PTSD Scale; CAPS-I = Clinician-Administered PTSD Scale Interview; CBT = cognitive behavioral therapy; COPE = Concurrent Treatment of PTSD and Substance Use Disorders Using Prolonged Exposure; CPT = cognitive processing therapy; CR = cognitive restructuring; EMDR = eye movement desensitization and reprocessing; F = female; G = group; HLS = health information control condition; IE = imaginal exposure; in vivo = in vivo exposure; MCT = metacognitive therapy; IRT = imagery rehearsal therapy; MET-PTSD = trauma-focused motivational enhancement therapy; mPE = modified prolonged exposure; MVA = motor vehicle accident; N = number; NR = not reported; PCT = present-centered therapy; PDS = Posttraumatic Diagnostic Scale; PE = prolonged exposure; PSS-I = PTSD Symptom Scale—Interview; PTSD = posttraumatic stress disorder; relax = relaxation; SC = supportive counseling; SIT = stress inoculation training; TAU = treatment as usual; UC = usual care; VRE = virtual reality exposure; WET = written exposure therapy; WL = wait-list; y = year.

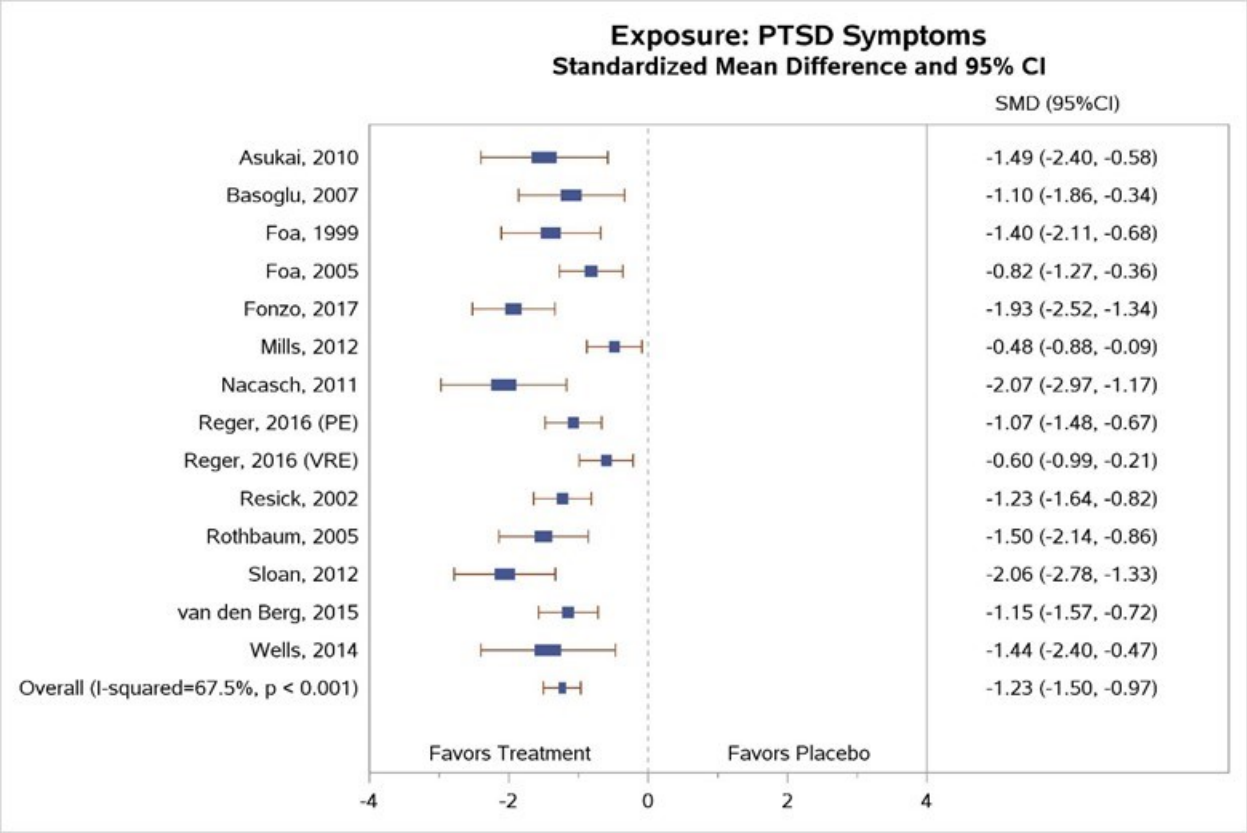
These studies generally enrolled subjects with severe or extreme PTSD symptoms.[10, 15, 19, 20, 41, 122, 133] Sample sizes ranged from 24 to 284. Four studies (one of which presented outcomes in 2 articles) assessed followup at the end of active treatment;[19-21, 132, 137] the remainder included posttreatment followups after 3, 4½, 6, 9, or 12 months. Fourteen of the studies enrolled a heterogeneous group of subjects with a variety of index trauma types (e.g., accident, disaster, physical assault, sexual assault, witnessing death or serious injury), 4 studies enrolled a majority of subjects with sexual assault-related PTSD,[3, 12-14] 4 enrolled subjects with combat-related PTSD,[15, 18, 139, 141] 1 enrolled subjects with combat- or terror-related PTSD,[15] 1 enrolled natural disaster victims,[11] and one enrolled patients involved in an MVA.[17] One involved patients with both a psychotic disorder and PTSD.[16] Mean age ranged from 27 to 63. Ten studies enrolled two-thirds or more female subjects. The primary outcome for the majority of studies was some version of the CAPS (CAPS, CAPS-2, or CAPS-Sx); 4 studies identified the PSS-I as the primary outcome measure;[12, 14, 15, 142] and 1 study used the PDS.[19]

Results for Exposure Therapy Compared With Inactive Comparators

PTSD Symptoms

Thirteen of the 14 studies (data for 1 study reported in 2 articles) comparing various exposure therapies with an inactive comparator reported measures of PTSD symptom change; one study compared each of two exposure therapies (VRE and PE) to placebo,[18] allowing 14 comparisons. All 13 studies reported outcomes in 14 publications reported greater decreases in PTSD symptoms (outcome measures included CAPS, PSS-I, and PDS) in the exposure group than in the control group.[3, 10-21, 137] Our meta-analysis of pooled data from these studies (Figure 7) found a greater decrease in PTSD symptoms for subjects treated with exposure than for those in control groups; the effect size was very large (SMD, -1.23; 95% CI, -1.50 to -0.97, 13 studies [14 comparisons]; N=885; I-squared, 67.5%; high SOE).

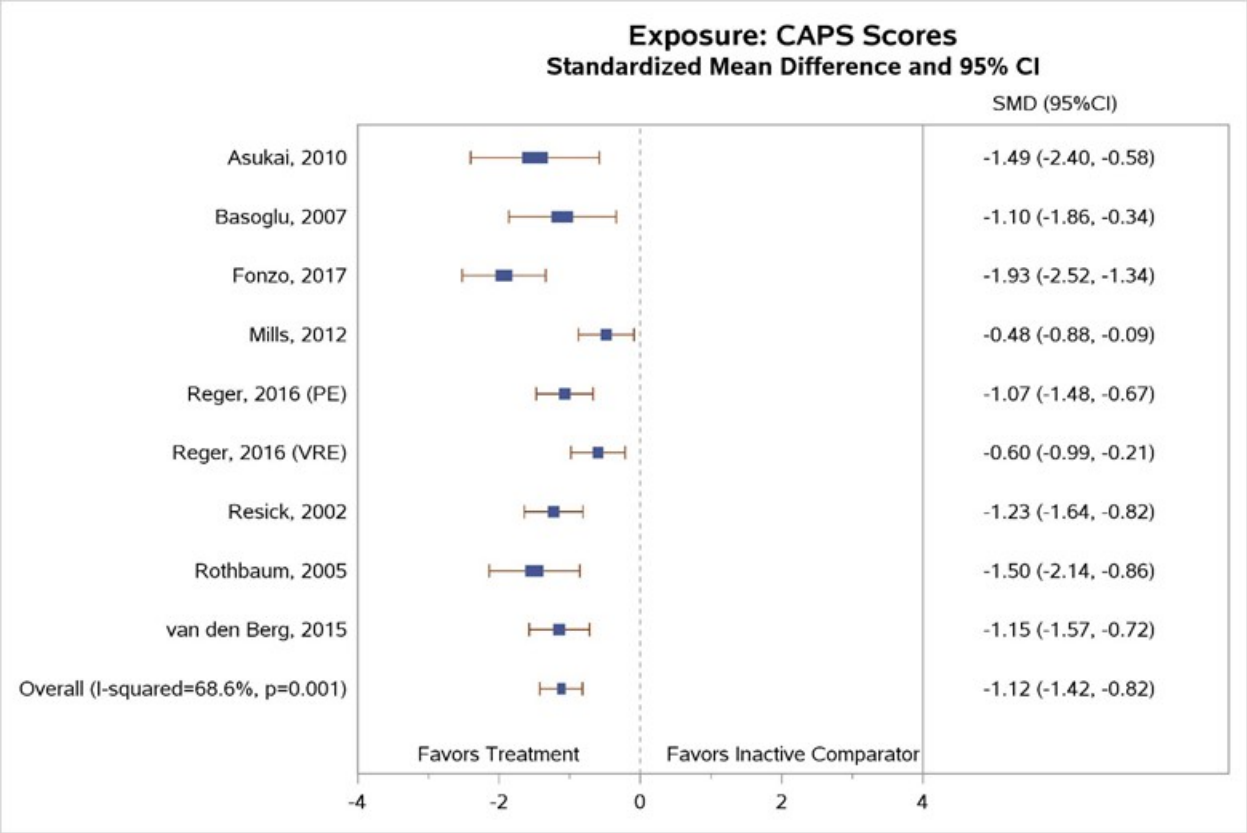
Figure 7. Standardized mean change from baseline to end of treatment in PTSD symptoms (any measure) for exposure therapy compared with inactive comparator



CI = confidence interval; PTSD = posttraumatic stress disorder; PE = prolonged exposure; SMD = standardized mean difference; VRE = virtual reality exposure.

Our meta-analysis of the studies reporting CAPS scores found a greater decrease in PTSD symptoms among subjects treated with exposure than those in an inactive comparator group (SMD, -1.12; 95% CI, -1.42 to -0.82; 8 studies [9 comparisons], N=689; I-squared=68.66%; high SOE) (Figure 8).

Figure 8. Standardized mean change from baseline to end of treatment in PTSD symptoms (CAPS) for exposure therapy compared with inactive comparator



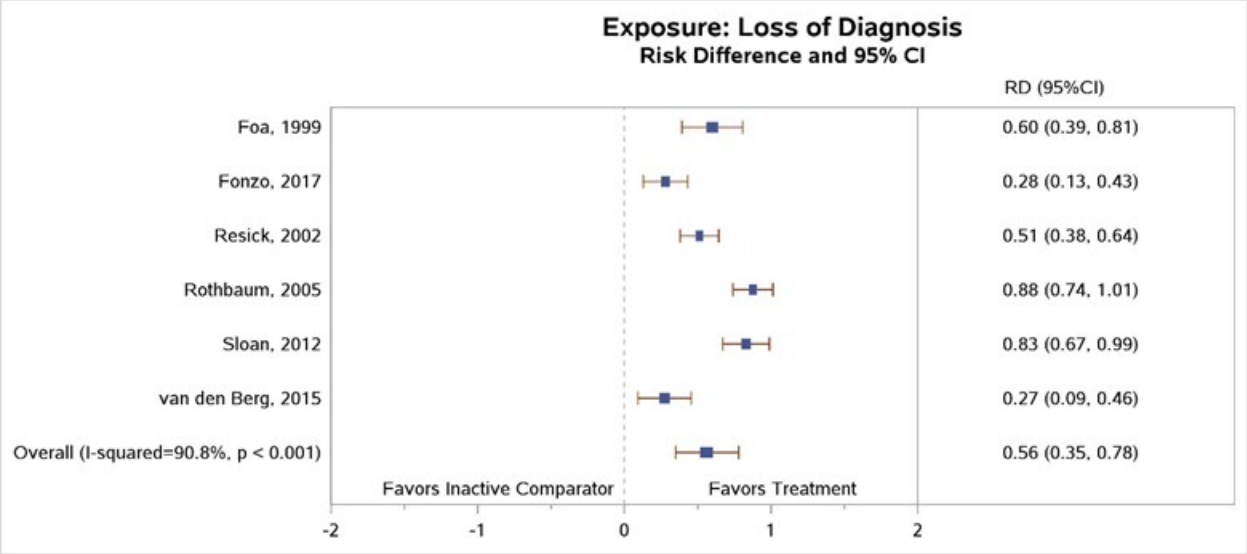
CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; PE = prolonged exposure; SMD = standardized mean difference; VRE = virtual reality exposure.

Among those studies that assessed followup measures longer-term, the effects for decreases in PTSD symptoms were maintained at 3, 6, 9, or 12 months.

Loss of PTSD Diagnosis

Six of the studies comparing subjects who received exposure therapy with those in inactive comparator groups reported loss of PTSD diagnosis between groups. Participants treated with exposure therapy had greater rates of loss of PTSD diagnosis as compared with participants in the inactive comparator groups (RD, 0.56; 95% CI, 0.35 to 0.78; 6 studies, N=409; high SOE) (Figure 9).

Figure 9. Loss of diagnosis for exposure therapy compared with inactive comparator



CI = confidence interval; RD = risk difference.

Prevention or Reduction of Comorbid Conditions

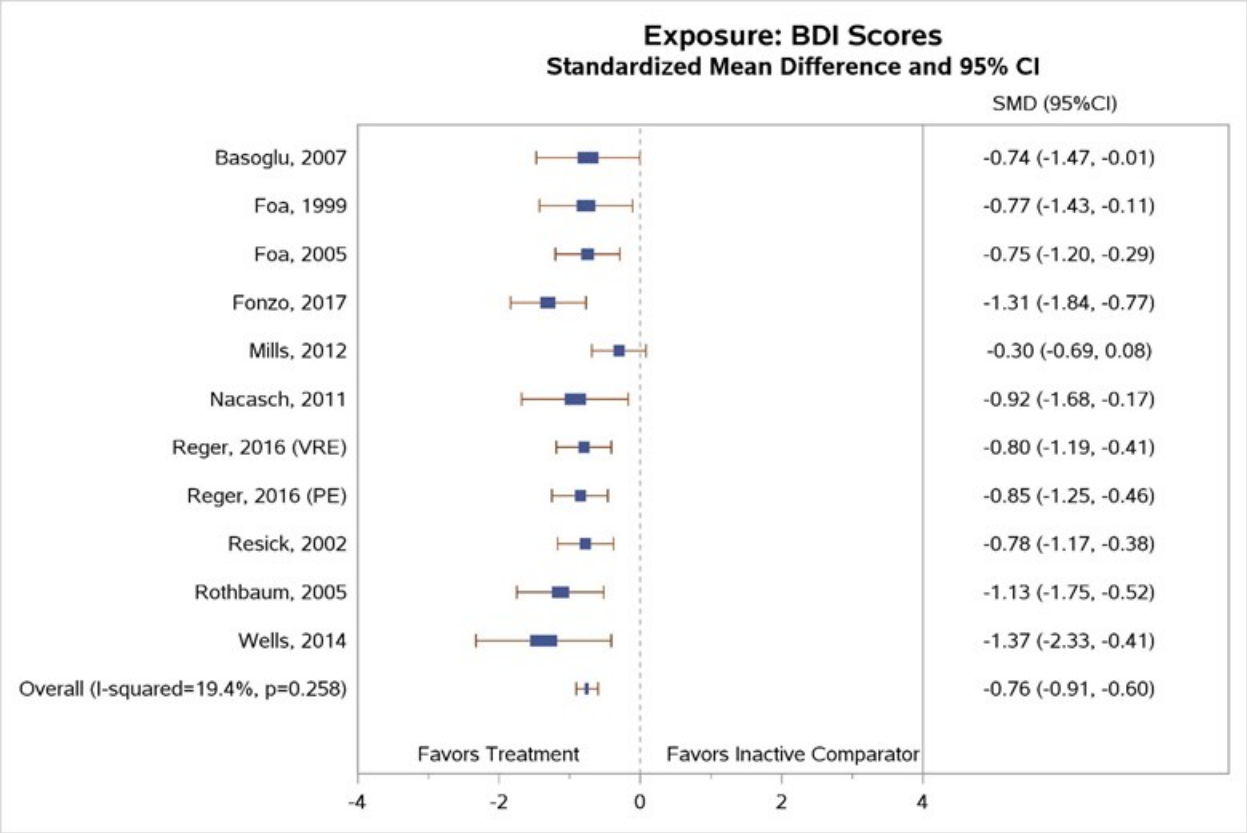
Ten studies (from 11 publications and involving 11 comparisons) with inactive comparators reported on changes in depression symptoms as measured by the BDI.[3, 11-15, 18-21, 137] All but 1[20] reported a significantly greater decrease in depression symptoms for exposure intervention patients than for inactive comparators. Results of our meta-analysis indicated a greater reduction in BDI depressive symptom scores for subjects treated with exposure than for those in wait-list or usual-care inactive comparator groups (SMD, -0.76; 95% CI, -0.91 to -0.60; I^2=19.4%, 10 studies [11 comparisons], N=7,152, Figure 10; high SOE).

Three studies reported on anxiety symptoms, two using the Beck Anxiety Inventory[18, 19] and one using the State Trait Anxiety Inventory.[20] The two using the Beck Anxiety Inventory indicated significant benefit for exposure therapy, while the study using the State Trait Anxiety Inventory (which involved patients with comorbid substance dependence) did not show significant benefit (low SOE).

Disability or Functional Impairment

Three studies compared functional impairment across groups using different scales (insufficient SOE). One study that compared in vivo exposure with wait-list included a measure of work and social adjustment and found significantly greater decreases in functional impairment in the in vivo group than the inactive comparator group.[11] Another study examined differences in four subscales of the World Health Organization Quality of Life brief version (WHOQOL-BREF) and found significantly greater increases in the physical health and psychological health (but not social relationships or environmental) subscales among those in the PE group than those in the wait-list control group.[21] A third study that compared PE, PE+CR, and wait-list that included the Social Adjustment Scale found greater, but not statistically significant, increases among the PE group subjects than the inactive comparator subjects (see Appendix F for details).[12]

Figure 10. Standardized mean change from baseline to end of treatment in depression symptoms (BDI) for exposure therapy compared with inactive comparator



BDI: Beck Depression Inventory; CI = confidence interval; PE = prolonged exposure; SMD = standardized mean difference; VRE = virtual reality exposure.

Results for Exposure Therapy Compared With Active Comparators

The 17 studies that compared exposure therapy with an active comparator included comparisons with EMDR,[13, 16, 133] a coping skills intervention (relaxation training[122, 132, 133] or SIT[14]), a cognitive intervention (CPT, CR, CT, or MCT),[3, 19, 122, 129] IPT,[132] PE+CR,[12, 42, 122] IE +CR,[41] PE plus SIT,[14] IRT[142] or another type of active control (PCT,[138, 139] relapse prevention,[143] active monitoring comparison group [AMCG],[143] supportive counseling [SC],[41] or a health information–based active control).[140]

In this section, we address the 17 studies comparing CBT-exposure therapy with an active comparator. We do not report on comparisons between exposure therapy arms and interventions for which we did not aim to assess comparative effectiveness (i.e., comparisons between different types of exposure interventions[39, 40, 144-148] or between exposure interventions and PCT, SC, relapse prevention, AMCG, or health information comparators).[3, 12-14, 16, 18, 19, 41, 42, 122, 129, 132, 133, 140, 143]

Results for Exposure Therapy Compared With Active Comparators: Exposure Therapy Versus Cognitive Interventions

Four studies compared exposure therapy and either CPT, CR, CT, or MCT.[3, 19, 122, 129] Of these, one compared PE with CR,[122] one compared IE with CT,[129] one compared PE with CPT,[3]

and one compared PE with MCT.[19] We did not perform quantitative meta-analysis to pool the findings because each intervention and comparator were different across each of the 4 studies.

PTSD Symptoms

The results from each different cognitive intervention-exposure intervention comparison found no significant differences in pre- to posttreatment PTSD symptom changes between groups;[3, 122, 129] results from one smaller study (11 patients per group) suggested greater benefit from MCT than PE (p=0.05; insufficient SOE).[19]

Loss of PTSD Diagnosis

Three studies testing different exposure interventions reported data on loss of PTSD diagnosis between exposure and cognitive intervention groups.[3, 122, 129] Two studies favored exposure (RD range 0.08 to 0.16), but differences were not significant;[122, 129] one found a zero RD between groups (insufficient SOE).[3]

Prevention or Reduction of Comorbid Conditions

All four studies used the BDI to measure change in depression symptom scores.[3, 19, 122, 129] Although point estimates favored CT and CPT over the exposure arms, no study found a statistically significant difference between the interventions (insufficient SOE).

Two studies compared anxiety symptoms between groups (insufficient SOE). One study found no significant differences between IE and CT groups at the end of treatment or 12-month followup assessments on BAI-assessed anxiety symptoms.[129] A second study also used the BAI to compare PE with MCT[19] and also found no statistically significant between-group differences (insufficient SOE).

Return to Work or Active Duty

One study of CT and IE reported the impact of interventions on return-to-work outcomes.[129] At 6 months followup, the difference in percentage working between treatment groups did not reach statistical significance (RD, 0.07; insufficient SOE).

Results for Exposure Therapy Compared With Active Comparators: Exposure Therapy Versus Coping Skills Therapies

Four studies compared exposure therapy with a coping skills therapy.[14, 122, 132, 133] One compared PE with SIT,[14] and the others compared PE with relaxation therapy.

PTSD Symptoms

All four studies compared PTSD symptom changes from pre- to posttreatment between exposure therapy and coping skills intervention groups.[14, 122, 132, 133] The results of our meta-analysis indicated that PE had greater decreases in PTSD symptoms than relaxation (SMD, -0.45; 95% CI, -0.78 to -0.13; 3 studies, N=155, moderate SOE). The study comparing PE with SIT found no significant between-group differences in decreases in PTSD symptoms at the end of treatment assessment (between-group mean difference, -1.8 favoring PE, insufficient SOE).[14]

Loss of PTSD Diagnosis

Two studies compared loss of PTSD diagnosis between CBT-exposure and relaxation group participants.[14, 122, 133] In each study, a greater proportion of subjects treated with CBT-exposure had loss of PTSD diagnosis at the end of treatment than subjects receiving each of the coping skills interventions (RD range 0.20 to 0.47 favoring CBT-exposure; moderate SOE).

The single study that compared loss of PTSD diagnosis between PE and SIT group subjects found no statistically significant difference between the two intervention groups (RD, 0.18; p=ns; insufficient SOE).[14]

Prevention or Reduction of Comorbid Conditions

Four studies compared CBT-exposure and CBT-coping interventions (relaxation or SIT) using BDI-related measures[14, 122, 133] or the Hamilton Depression Rating Scale (HAM-D) to assess depression symptoms.[132] The single study comparing exposure with SIT found no difference in depression symptom changes between treatments at the end of treatment (insufficient SOE).[14]

The meta-analysis of the three studies that compared CBT-exposure (PE) with relaxation therapy,[122, 132, 133] found that PE had greater decreases in depressive symptoms than relaxation (SMD, -0.39; 95% CI, -0.71 to -0.07; 3 studies, N=155, moderate SOE).

Results for Exposure Therapy Compared With Active Comparators: Exposure Therapy Compared With Eye Movement Desensitization and Reprocessing

PTSD Symptoms

All three studies[13, 16, 133] that compared PE with EMDR found no statistically significant difference in pre- to posttreatment PTSD symptom changes between EMDR and PE intervention groups (meta-analysis not performed for any of the PE versus EMDR pooled findings because of substantial heterogeneity in intervention characteristics and sample characteristics, low SOE for no difference).

Loss of PTSD Diagnosis

Three studies compared the effectiveness of PE versus EMDR on loss of PTSD diagnosis with different results (insufficient SOE). In two studies, more participants in the PE group than in the EMDR group lost their PTSD diagnosis at posttreatment, but differences were not statistically significant (RD range 0.20 to 0.28 across 2 studies, p=ns[13, 133]). In contrast, in another study, slightly fewer participants in the PE group lost their PTSD diagnosis than in the EMDR group (RD=0.03, p=ns).[16]

Prevention or Reduction of Comorbid Conditions

Two studies used the BDI to assess change in depression symptom scores. In both studies, PE and EMDR did not have statistically significant differences in the reduction of depression symptoms between groups (insufficient SOE).[13, 133]

Results for Exposure Therapy Compared With Active Comparators: Exposure Therapy Versus Exposure Plus Cognitive Restructuring

Four studies compared exposure therapy with exposure+CR.[12, 41, 42, 122] Three tested PE against PE+CR,[12, 42, 122] whereas the other tested IE against IE+CR.[41]

PTSD Symptoms

Two studies found no difference between subjects treated with exposure and those treated with PE+CR on measures of PTSD symptoms (insufficient SOE).[12, 122] Another study found no significant difference at the end of treatment but an advantage for IE plus CR at posttreatment followup (insufficient SOE).[41] Finally, one study found that exposure plus CR led to significantly greater decreases in PTSD symptoms at the end of treatment as compared with exposure alone (insufficient SOE).[42]

Loss of PTSD Diagnosis

Three of these four studies reported data on loss of PTSD diagnosis between groups at posttreatment.[41, 42, 122] One study favored the PE group,[122] and the other two favored the combined PE+CR group (meta-analysis not performed for exposure versus exposure plus CR findings because of heterogeneity in intervention and sample characteristics, insufficient SOE).[41, 42]

Prevention or Reduction of Comorbid Conditions

All four studies used the BDI to assess depression symptoms. Each found no statistically significant difference between interventions from baseline to the end of treatment (low SOE for no difference).

Results for Exposure Therapy Compared With Active Comparators: Prolonged Exposure Versus Interpersonal Psychotherapy

As noted above, one study compared PE (N=38), IPT (N=40), and relaxation (N=32).[132] We previously compared exposure and relaxation; here, we report the PE versus IPT comparison (insufficient SOE for each outcome). Both types of interventions led to substantial decreases in PTSD symptoms at posttreatment, but the authors found no significant between-group differences. In addition, the proportions of subjects who entered remission did not differ (RD=0.03); the groups also did not differ with respect to decreases in depressive symptoms as measured by the HAM-D or changes in quality-of-life ratings as measured by the Quality of Life Enjoyment and Satisfaction scale.[132] We concluded that evidence is insufficient to determine the comparative effectiveness of PE versus IPT for PTSD symptoms, remission, depressive symptoms, and quality of life based on this single study.

Results for Exposure Therapy Compared With Active Comparators: Prolonged Exposure Versus Imagery Rehearsal Therapy

One study compared PE and IRT.[142] Significant differences were not found for decreases in PTSD symptoms, percentage recovering or with symptom improvement, or decreases in depression symptoms or psychological symptom severity between treatment groups. The treatment* time interaction for the psychological subscale of the quality of life assessment scale approached significance (p=0.05), with the PE group participants having slightly greater improvements at posttreatment that evened out at the 3-month followup assessment. We

concluded that evidence is insufficient to determine the comparative effectiveness of PE versus IRT for PTSD symptoms, remission, depressive symptoms, and quality of life based on this single study.

Detailed Synthesis: CBT—Mixed Interventions

Characteristics of Studies

Table 12 summarizes the characteristics of the 31 studies meeting our inclusion criteria. Further details about these studies appear in Appendix D. The studies in this section are somewhat heterogeneous in several ways: how authors define and describe "cognitive behavioral therapy," duration of the intervention, and mode of delivery. Elements of the CBT arm of the studies considered here include psychoeducation, self-monitoring, stress management, relaxation training, skills training, exposure (imaginal, in vivo, or both), cognitive restructuring, guided imagery, mindfulness training, breathing retraining, crisis/safety planning, and relapse prevention. The studies varied as to how many sessions (if any) were dedicated to these elements and whether homework was assigned as part of the intervention.

Table 12. Characteristics of included CBT-mixed intervention trials

Study	Arm (N)	Duration tx (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Acosta et al., 2017[149]	Web CBT plus UC (81) UC (81)	12 weeks (post, 1 month, 3 months)	Combat veterans with PTSD and substance abuse 79% of sample had clinical PTSD	78.6	32	7	13	Medium
Blanchard et al., 2003[36]	CBT-M (27) SC (27) WL (24)	8 to 12 weeks (3 months)	Male and female MVA 83% of sample had clinical PTSD	65.0 to 68.2	41	73	10.2	Medium
Bohus et al., 2013[23]	DBT (43) UC-WL (39)	24 weeks (post, 6 weeks, 12 weeks)	Child abuse survivors with and without borderline personality disorder	83 to 88	36	100	NR	Medium
Bryant et al., 2003[41]	IE (20) CBT-M[b] (IE+CR) (20) SC (18)	8 weeks (6 months)	Male and female Mixed	CAPS-I 32.5 to 32.9 CAPS-F 36.0 to 38.3	35	52	NR	Medium
Bryant et al., 2008[42]	PE (31) CBT-M[b] (exp+CR) (28) IE (31) In vivo (28)	8 weeks (6 months)	Male and female Mixed	71.4 to 76.8	37	NR	8	Medium
Cloitre et al., 2002[37]	CBT-M (31) WL (27)	12 months	Female Childhood abuse	69	34	100	54	Medium

Study	Arm (N)	Duration tx (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Cloitre et al., 2010[148] Cloitre et al., 2016[150]	CBT-M (33) CBT-M (38) CBT-M (33)	16 weeks (3 and 6 months)	Female Mixed childhood abuse	63.1 to 64.5	36	100	64	Medium
Cottraux et al., 2008[31]	CBT-M (31) SC (29)	16 weeks (1 and 24 months)	Male and female Mixed	PCLS 60.8	39	70	NR	Medium
Engel et al., 2015[26,c*]	Online CBT and stress inoculation training, nurse guided (43) Optimized UC (37)	6 weeks (post [6 weeks], 12 weeks, 18 weeks)	Veterans of recent military conflicts PTSD	PCL 58.56 to 55.16	36	19	45	Medium
Fecteau et al., 1999[38]	CBT-M (22) WL (21)	4 weeks (6 months)	Male and female MVA	70.9 to 77.3	41	70	NR	Medium
Foa et al., 1999[14] Zoellner et al., 1999[134]	PE (25) SIT (26) CBT-M[b] (PE+SIT) (30) WL (15)	9 weeks (3, 6, and 12 months)	Female Assault	PSS-I 29.4 to 32.9	35	100	36	Medium
Foa et al., 2005[12]	Total 190 PE (NR) CBT-M[b] (PE+CR) (NR) WL (NR)	12 weeks, 9 to 12 weekly sessions (3, 6, and 12 months)	Female Assault	PSS-I 31.1 to 34.0	31	100	51	Medium
Haller et al., 2016[145,c]	Group ICBT for depression and SUD plus CPT-M (trauma-focused CPT modified to include substance use prevention) (individual) (61) Group ICBT for depression and SUD plus individual ICBT for depression and SUD (62)	12 sessions (up to 16 weeks) (post, 3 months, 6 months, 9 months, 12 months)	Veterans with MDD or dysthymia, past 90-day alcohol, cannabinoid, or stimulant dependence, and trauma exposure 82.1% of sample had clinical PTSD	PCL 56.99	47	11	36	Medium
Harned et al., 2014[144]	DBT plus DBT PE (17) DBT (9)	1 year (3 months)	PTSD with borderline personality disorder and intentional self-injury	PSS-I 30 to 33	33	100	19	Medium
Hinton et al., 2005[34]	CBT-M (20) WL (20)	12 weeks	Male and female Cambodian refugees	74.9 to 75.9	52	60	100	Medium

Study	Arm (N)	Duration tx (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Hinton et al., 2009[151]	CBT-M (12) CBT-M (12)	12 weeks	Cambodian refugees Witnessed genocide	75.4 to 77.3	50	60	100	Medium
Hinton et al., 2011[152]	CBT-M (12) Relax (12)	14 weeks (12 weeks)	Female Trauma NR	PCL 69.8 to 71.1	50	100	100	Medium
Hollifield et al., 2007[32]	Acupuncture (29) (arm not eligible) CBT-M (28) WL (27)	12 weeks (3 months)	Male and female Mixed	PSS-SR 30.8 to 32.5	42	48	24	Medium
Ivarsson et al., 2014[24]	Internet-based CBT (31) Delayed treatment (WL) attention control (31)	8 weeks (post)	Chronic PTSD Mixed	IES-R 55	46	82	NR	Medium
Johnson et al., 2011[29]	CBT-M (35) UC (35)	8 months (1 week, 3 and 6 months)	Female Interpersonal violence 87% of sample had clinical PTSD	53.3 to 62.7	33	100	57	Medium
Kubany et al., 2003[35]	CBT-M (19) WL (18)	8 to 11 sessions[d] (3 months)	Female Interpersonal violence	80.1 to 80.2	35	100	51	Medium
Kubany et al., 2004[28]	CBT-M (63) WL (62)	4 to 5.5 weeks (3 and 6 months)	Female Interpersonal violence	74.1 to 74.4	42	100	47	Medium
Litz et al., 2007[33]	CBT-M (24) SC (21)	8 weeks (3 and 6 months)	Male and female Combat	PSS-I 26.7 to 29.2	39	22	30	Medium
Maguen et al., 2017[25]	CBT (17) WL (16)	6 weeks (post)	Endorsed killing or responsible for the death of another in a war zone, PTSD	PCL 48.6 to 52.9	61	0	39	Medium

Study	Arm (N)	Duration tx (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Marks et al., 1998[122] Lovell et al., 2001[123]	PE (23) CR (13) CBT-M[b] (CR+PE) (24) Relax (21)	10 sessions[d] (mean of 16 weeks), (1, 3, and 6 months)	Male and female Mixed	CAPS Severity 2.6 to 3.2	38	36	NR	Medium
McDonagh et al., 2005[39]	CBT-M (29) PCT (22) WL (23)	14 weeks (3 and 6 months)	Female Childhood sexual abuse	67.7 to 72.0	41	100	7	Medium
McGovern et al., 2015[27,c]	ICBT for PTSD and SUD plus SC (73) IAC plus SC (75) (arm not eligible) Standard care (73)	8–12 sessions typically completed in 8–12 weeks (post at 6 months post-baseline)	PTSD and substance abuse	77.35	35	59	4	Medium
Monson et al., 2012[22]	CBCT (20 individuals) WL (20 individuals)	15 sessions (3 months after treatment)	Veterans and their partners	68.87 to 73.03	37	75	28	Medium
Sannibale et al. 2013[146]	IT (integrated CBT for PTSD and AUD) (33) CBT for AUD plus SC (29)	12 weeks (post, 5 months, 9 months)	Comorbid PTSD and AUD	68	41	53	NR	Low
Spence et al., 2011[30]	CBT-M (23) WL (21)	8 weeks (3 months)	Male and female Mixed	PCL-C 57.0 to 60.8	43	81	NR	Medium
van Emmerik et al., 2008[40]	CBT-M (41) Writing (44) WL (40)	5 sessions[d] (mean of 17 weeks), 13 to 139 weeks	Male and female Mixed 97% of sample had clinical PTSD	IES 46.4 to 49.1	40	67	NR	Medium

[a] Data reported are mean CAPS or range of mean CAPS scores across groups unless another instrument is specified.
[b] The information provided after CBT-M indicates the content of the mixed intervention (see abbreviations below).
[c] Less than 100 percent of sample had clinical PTSD.
[d] Number of treatment sessions is reported when duration of treatment was not specified.

AUD = Alcohol Use Disorder; CAPS = Clinician-Administered PTSD Scale; CBCT = cognitive behavioral couples therapy; CBT-M = cognitive behavioral therapy-mixed; CR = cognitive restructuring; DBT = dialectical behavior therapy; F = female; IAC = individual addiction counseling; ICBT = integrated cognitive behavioral therapy; IE = imaginal exposure; IES = Impact of Event Scale; in vivo = in vivo exposure; IT = integrated treatment; MDD = major depressive disorder; MVA = motor vehicle accident; NR = not reported; PCL = Posttraumatic Stress Disorder Checklist; PCL-C = Posttraumatic Stress Disorder Checklist-Civilian Version; PCLS = Post-Traumatic Stress Disorder Checklist Scale; PDS = Posttraumatic Stress Diagnostic Scale; PE = prolonged exposure; PSS-I = PTSD Symptom Scale—Interview; PSS-SR = Posttraumatic Symptom Scale-Self Report; PTSD = posttraumatic stress disorder; relax = relaxation; SC = supportive counseling; SIT = stress inoculation training; SUD = substance use disorder; UC = usual care; WL = wait-list; writing = structured writing therapy; y = year.

Twenty-three of these 31 studies included an inactive comparator, such as a wait-list (16 studies), usual care (4 studies), or SC (4 studies).[12, 14, 22-41, 149] Thirteen of the 31 studies made

comparisons with active interventions (i.e., other psychotherapies).[12, 14, 39-42, 122, 144-146, 148, 151, 152] Of these 13 studies, 5 included an exposure-based intervention as the comparison;[12, 14, 41, 42, 122] 1 used structured writing therapy (SWT);[40] 1 used PCT;[39] 2 used relaxation;[122, 152] 2 used another CBT-mixed intervention;[148, 151] 1 used a CBT for Alcohol Use Disorder (AUD) plus SC;[146] 1 used a group integrated cognitive behavioral therapy (ICBT) for depression and substance use disorder (SUD) followed by individual ICBT for depression and SUD;[145] and 1 study that tested a dialectical behavior therapy-(DBT)-PE combination therapy used DBT alone as the comparison group.[144]

Of the 24 studies with *inactive* comparators, sample sizes ranged from 23 to 190. Duration of treatment ranged from 4 to 24 weeks. Although 3 studies did not include a followup assessment[22, 24, 25] and the followup interval for 1 was unclear,[40] the remainder of the studies with *inactive* comparators included at least one posttreatment followup assessments after 1 to 12 months.[40] The majority of studies enrolled a heterogeneous group of subjects with a variety of index trauma types and comorbid mental health problems (e.g., depression, personality disorders, SUD/AUD). Mean age ranged from 30 to 61 years. Most studies enrolled a large majority of female subjects. The primary outcome measure for 13 of these studies was some version of the CAPS (CAPS, CAPS-2, or CAPS-Sx);[22-24, 27-29, 34-39, 41] 4 studies used a form of the PSS (PSS-I or PSS-SR);[12, 14, 32, 33] 3 studies used the PDS;[23, 24] 5 studies used the PCL;[25, 26, 30, 31, 149, 153] and 2 the IES.[24, 40]

Of the 13 studies with *active* comparators,[40-42, 122] sample sizes ranged from 24 to 190. Duration of treatment ranged from 8 to 16 weeks, with the exception of the study testing DBT-PE vs. DBT,[144] where treatment lasted for 1 year. All studies also included posttreatment followup assessments ranging from 1 to 12 months. The majority of studies enrolled a heterogeneous group of subjects with a variety of index trauma types and comorbid mental health conditions (e.g., depression, SUD/AUD, personality disorders, intentional self-injury). Mean age ranged from 33 to 50. Most studies enrolled a large majority of female subjects. The primary outcome for 6 studies was some version of the CAPS (CAPS, CAPS-2, or CAPS-Sx); 3 used the PSS-I,[12, 14, 146] 2 used the PCL,[144, 152] 1 used the PDS,[146] and 1 used the IES.[40]

Results for CBT-Mixed Interventions Compared With Inactive Comparators

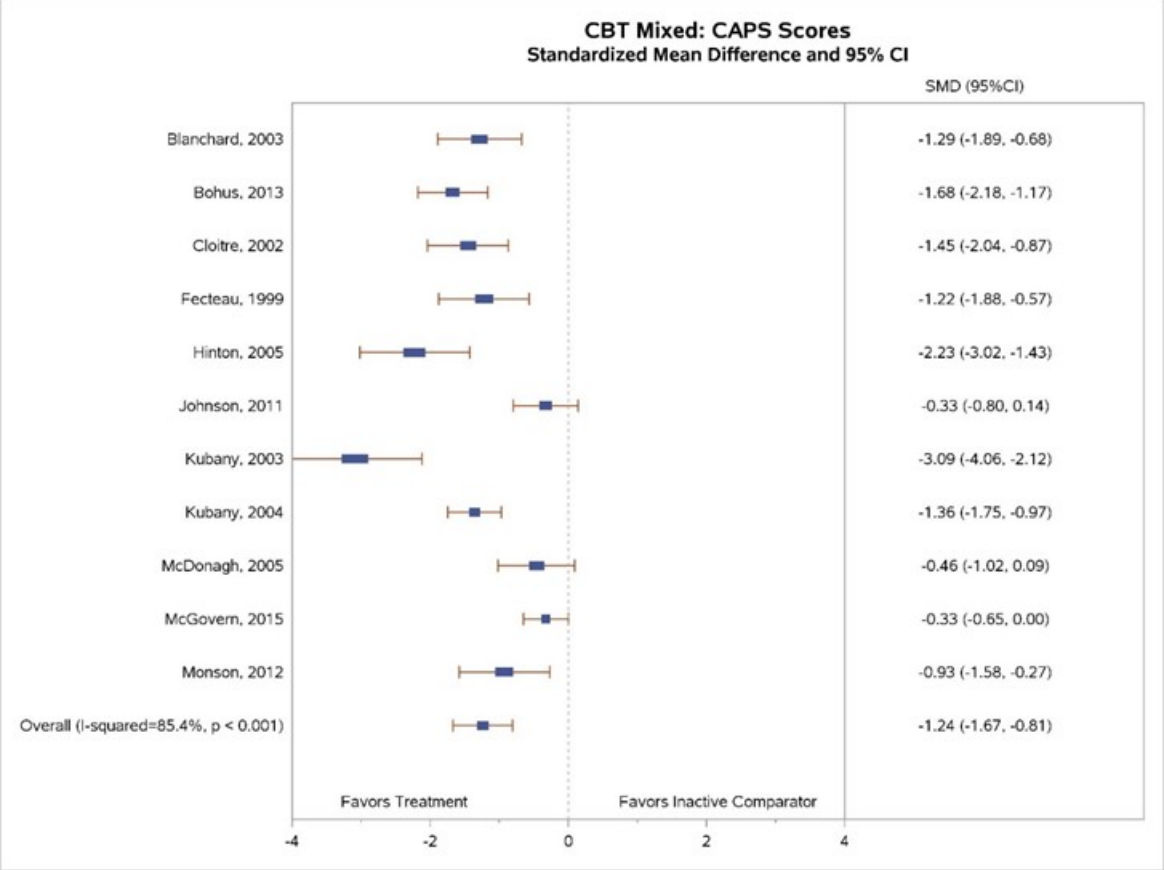
PTSD Symptoms

Of the 23 studies with inactive comparators, 21 compared PTSD symptom changes pre- to posttreatment between CBT-M and inactive comparator groups, half (n=11) of which used the CAPS to report outcomes. Among the 11 studies that used the CAPS, 8 reported decreases in PTSD symptoms as assessed by the CAPS that were statistically significant. Full evidence tables from each of these studies can be found in Appendix F.

Our meta-analysis (Figure 11) found greater decreases in CAPS-rated PTSD symptoms for CBT-M interventions than for inactive controls (SMD, -1.24; 95% CI, -1.67 to -0.81; 11 studies, N=709; high SOE). Statistical heterogeneity was substantial (I^2=85.4%). Much of the heterogeneity may be explained by the diversity of both interventions (as explained above, these interventions used various CBT components). Six studies found a similarly large decrease in PTSD scores assessed by CAPS for CBT-M intervention groups compared with wait-list or usual-care controls—about a 30-point greater reduction.[23, 28, 34, 36-38] One study with a wait-list control found even greater decreases (about a 68-point decrease).[35] Three of the 10 studies found

little to no decrease.[27, 29, 39] One of these compared CBT-M interventions with usual care (in which the control patients were often receiving some form of treatment)[29] and another with standard care[27] rather than with wait-list; this likely biased results toward the null.

Figure 11. Mean change from baseline in CAPS for CBT-mixed interventions compared with inactive comparators



CAPS = Clinician-Administered PTSD Scale; CBT = cognitive behavioral therapy; CI = confidence interval SMD = standardized mean difference.

We conducted additional meta-analyses to pool pre- to posttreatment differences in PTSD symptoms across groups using additional outcome measures reported across all studies with inactive comparators (CAPS, PSS-I, IES, PCL, PDS). Our meta-analysis found greater decreases in PTSD symptoms for CBT-mixed interventions compared with inactive controls (SMD, -1.01; 95% CI, -1.28 to -0.74; 21 studies, N=1,349, Appendix H; high SOE). Similar to the CAPS meta-analysis, statistical heterogeneity was substantial (I^2=81.1%). However, also like the synthesis of CAPS data, the differences in findings were in the magnitude (not the direction) of the effect; all point estimates favored CBT-mixed interventions, and the vast majority of individual studies reached statistical significance.

Three of the 10 studies reported data on PTSD symptoms assessed by CAPS at 3- to 6-month followups (Appendix H).[23, 29, 36] Of these, 2 found significant between-group differences favoring the CBT-mixed intervention over inactive comparators,[23, 36] and the other study found no significant differences between groups.[29] These findings mirrored those found at the end of treatment assessments.

Adding three additional studies that used PTSD symptom measures other than the CAPS to the analysis permitted pooled analysis via meta-analysis. Of the six studies, four found statistically significant between-group differences from pretreatment to followup assessment, favoring CBT-mixed interventions over wait-list[23, 32, 36] and SC groups;[33] two studies found no significant pretreatment to followup assessment between a CBT-mixed intervention and wait-list[26] or usual care (Appendix H).[29] Meta-analysis of the six studies found that between-group differences in PTSD symptom changes persisted after the end of treatment but with a somewhat smaller effect size than found at the posttreatment assessment (SMD, -0.8; 95% CI, -1.3 to -0.2; Appendix H; high SOE). Determining with confidence how much of the between-group differences in PTSD symptom decreases persist at longer-term followup is difficult, partly because of the potential for reporting bias (i.e., studies not reporting followup data because the significant differences did not persist).

Remission

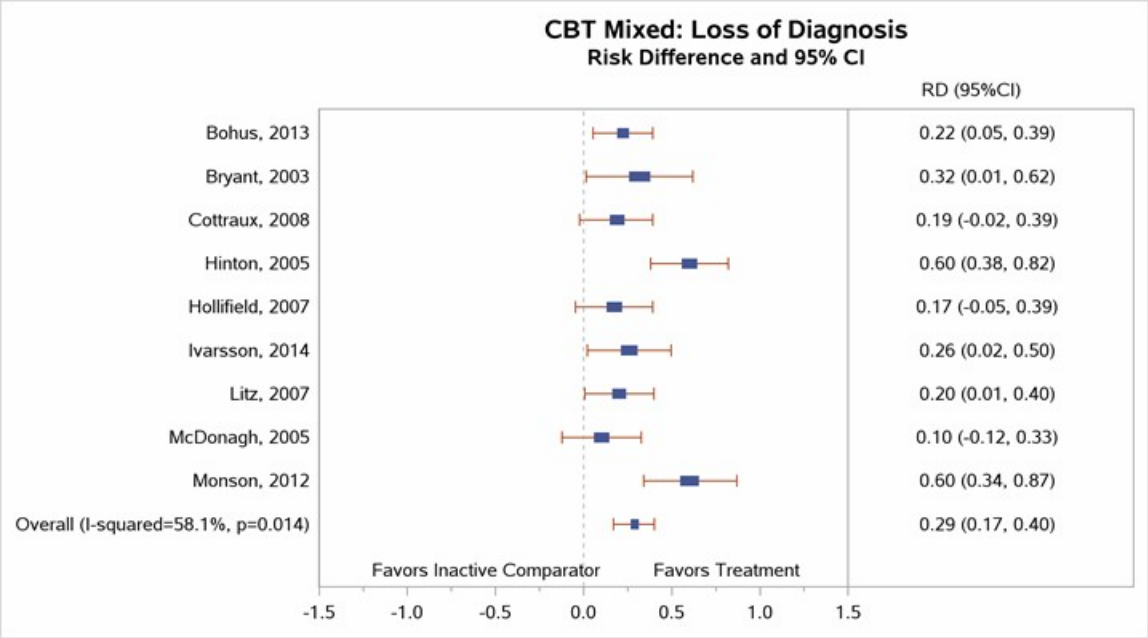
One small CBT-mixed study reported that a greater percentage of subjects in the CBT-mixed group achieved remission compared with inactive comparator subjects (RD=0.40 using the PCL,[30] insufficient SOE).

Loss of PTSD Diagnosis

Nine studies reported sufficient data on loss of PTSD diagnosis to permit meta-analysis.[22-24, 31-34, 39, 41] Our meta-analysis (Figure 12) found a large effect size (RD, 0.29; 95% CI, 0.17 to 0.40; I^2=58.1%, 9 studies, N=474) for loss of PTSD diagnosis between CBT-mixed and inactive comparator subjects (high SOE).

Two of the studies also reported 3- to 6-month loss of PTSD diagnosis followup data.[33, 41] Significant findings from both studies suggested that the between-group differences in loss of PTSD diagnosis favoring the CBT-mixed interventions over inactive comparators persisted over time.

Figure 12. Loss of PTSD diagnosis for CBT-mixed interventions compared with inactive comparator



CBT = cognitive behavioral therapy; CI = confidence interval; RD = risk difference.

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Fifteen of the 24 studies that compared CBT-mixed interventions with an inactive control reported data on depression symptoms using the BDI. All but one of these reported point estimates favoring subjects treated with CBT-mixed interventions; the vast majority reported these findings to be statistically significant. Meta-analysis of these studies found greater improvement in depression symptoms for subjects treated with CBT-mixed interventions than for those in inactive comparator (SMD, -0.87; 95% CI, -1.14 to -0.61; I^2=72.0%, 15 studies, N=929; Appendix H; high SOE).

Five of the studies reported sufficient 3- to 6-month postintervention followup data for between-group changes in depressive symptoms. Meta-analysis of the five studies found that improvements were maintained but with a slightly smaller effect size (SMD, -0.55; 95% CI, -0.78 to -0.31; 5 studies, N=286, moderate SOE, Appendix H).

A number of studies also reported reduction in anxiety symptoms; a variety of different measures were used. The most commonly reported measure was the STAI, reported by five of the studies that compared CBT-mixed interventions with an inactive comparator. Most found greater decreases in anxiety symptoms for subjects treated with CBT-mixed interventions than for those in inactive comparator groups. Meta-analysis of these studies found greater between-group decreases in anxiety symptoms among subjects treated with CBT-mixed interventions than those in inactive comparator groups from pre- to posttreatment (SMD, -0.79; 95% CI, -1.31 to -0.27; 5 studies, N=257; I squared=82.9; Appendix H; moderate SOE).

A few studies testing interventions targeting individuals with comorbid PTSD and substance use problems reported on various substance use outcome measures using a wide variety of measures. One study of veterans with comorbid PTSD and SUD found the CBT-M group had a lower mean percentage of heavy drinking days at posttreatment than controls;[149] another found significant decreases in positive toxicology tests and self-reported amount and frequency of substance use among CBT-M group participants as compared with controls (moderate SOE).[27]

Quality of Life

Five studies reported data on quality of life.[24, 26, 31, 39, 149] The use of four different quality-of-life measures[149] across the five studies (one of which included only subscale data[149]), however, precluded the use of meta-analysis to pool findings.[149]

The five studies had mixed findings (insufficient SOE). Three studies found no differences between groups,[26, 39, 149] and two studies reported greater improvements among CBT-mixed participants than inactive control participants.[24, 31] Taken together, this evidence is insufficient to determine the efficacy of CBT-mixed interventions for improving quality of life.

Disability or Functional Impairment

Six studies reported data on disability or functional impairment[23, 30-32, 36, 37] using a variety of measures (Table 13). We did not use meta-analysis to pool findings because of the diversity of measures that did not assess the same types of disability and functional impairment. Four of the six studies found significantly greater improvements in disability or functional outcomes for those who received CBT-mixed interventions than those who received an inactive control (low SOE).

Table 13. Results at the end of treatment for disability or functional impairment outcomes for CBT-mixed interventions compared with inactive controls

Study	Arm (N)	Outcome Measure(s)	Baseline Value	End of Treatment Value	Change From Baseline	P-Value	Effect Size (Cohen's d)
Blanchard et al., 2003[36]	CBT-M (27) WL (24)	GAF	CBT-M: 53.9 WL: 56.0	75.8 60.4	NR	<0.05	NR
Bohus et al., 2013[23]	CBT-M (43) UC-WL (39)	GAF	CBT-M: 41.50 WL: 42.79	CBT-M: 49.44 WL: 43.79	NR	<0.01	NR
Cloitre, 2002[37]	CBT-M (31) WL (27)	IIP SAS-SR ISEL	CBT-M: 1.88 WL: 1.70 CBT-M: 2.44 WL: 2.57 CBT-M: 24 WL: 23	CBT-M: 1.06 WL: 1.60 CBT-M: 2.06 WL: 2.47 CBT-M: 30 WL: 23	NR	0.01 0.02 0.01	NR
Cottraux et al., 2008[31]	CBT-M (31) SC (29)	Global Phobic Disability Subscale of FQ	NR	4.4 4.0	-2.14 -2.0	0.86	NR
Hollifield et al., 2007[32]	Acupuncture (29) (intervention not eligible) CBT-M (28) WL (27)	SDI	CBT-M: 4.09 WL: 4.0	3.3 3.96	NR	<0.05	0.76 0.04
Spence et al., 2011[30]	CBT-M (23) WL (21)	SDS	CBT-M: 18.17 WL: 19.42	13.22 18.11	NR	0.07	0.62

Note: Results are only presented for the relevant arms for this section (CBT-M and inactive comparators); values entered are means unless otherwise specified; p-values are for the comparison between CBT-M and inactive comparators.

CBT-M = cognitive behavioral therapy mixed; FQ = Fear Questionnaire (a self-rating inventory for evaluation of agoraphobia, social phobia, blood-injury phobia, anxiety-depression, and global phobic disability); GAF = Global Assessment of Functioning; IIP = Inventory of Interpersonal Problems; ISEL = Interpersonal Support Evaluation List; N = number; NR = not reported; SAS-SR = Social Adjustment Scale-Self Report; SC = supportive counseling; SDI = Sheehan Disability Inventory; SDS = Sheehan Disability Scale; UC = usual care; WL = wait-list.

Results for CBT-Mixed Interventions Compared With Active Comparators

Of the 12 studies comparing a CBT-mixed intervention with an active comparator, 5 compared a CBT-mixed intervention against an exposure-based intervention.[12, 14, 41, 42, 122] Assessment of head-to-head comparisons with exposure-based interventions is covered in the CBT—Exposure section (above). Several of the other studies made comparisons with interventions for which we did not aim to assess comparative effectiveness[39, 40, 144-146, 148] (e.g., comparisons with other CBT-mixed interventions,[144-146, 148] SWT,[40] or an active control [PCT].[39] In this section, we address the 2 studies comparing CBT-mixed interventions and relaxation interventions.[122, 152]

Results for CBT-Mixed Interventions Compared With Active Comparators: CBT-Mixed Versus Relaxation

PTSD Symptoms

Both studies that evaluated CBT-M versus relaxation reported significantly greater decreases in PTSD symptoms among CBT-mixed intervention participants than relaxation participants (low SOE).[122, 152] One reported large between-group differences in PTSD symptoms assessed by the CAPS (between-group mean difference, -24), and the other reported a large between-group effect size (between-group mean difference, -21.2) in PCL-measured PTSD symptoms between groups that persisted[122] at followup ($p<0.05$).

Disability or Functional Impairment

One study reported data on disability or functional impairment using the General Health Questionnaire (GHQ) Global Improvement measure (insufficient SOE).[122] A greater (but not statistically different) percentage of subjects in the CBT arm than in the relaxation arm showed improvements in functioning (RD, 0.15; p=NS).

Detailed Synthesis: Eye Movement Desensitization and Reprocessing

Characteristics of Studies

Table 14 summarizes the characteristics of the 10 studies meeting our inclusion criteria. Further details describing the included studies are provided in Appendix F. Eight studies had an inactive comparator, such as wait-list,[13, 16, 44-46, 48] "stabilization as usual,"[43] or placebo.[47] Five had active comparisons with either PE,[13, 16, 133] BEP,[154] or relaxation training.[46, 133]

Sample sizes ranged from 21 to 155. Duration of treatment ranged from 4 to 8 weeks. Although one study did not include a followup assessment[48] and another included only a followup at 5 weeks posttreatment, the rest of the EMDR studies included posttreatment followups after 3, 6, or 9 months. Two of the studies enrolled a heterogeneous group of subjects with a variety of index trauma types (e.g., sexual assault, physical assault, witnessing traumatic events, accidents, and combat), one study enrolled a majority of subjects with combat-related PTSD,[46] one enrolled Swedish public transportation workers who witnessed train accidents or were physically assaulted,[48] two enrolled female victims of sexual assault,[13, 45] two enrolled refugees,[43, 44] and one enrolled participants with comorbid psychotic disorders with mixed

Table 14. Characteristics of included EMDR trials

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Acarturk et al., 2016[44]	EMDR (49) WL (49)	2 to 7 sessions (time to complete not specified) (1 week post-tx, 5 weeks)	Refugees	IES-R 50 to 62	34	74	100	Medium
Carlson et al.,1998[46]	EMDR (10) Relaxation (13) WL (12)	Twice a week for 6 weeks (3 and 9 months)	Male Vietnam combat veterans	M-PTSD 117.9 to 119.4	49	0	46	Medium
Hogberg et al., 2007[48]	EMDR (13) WL (11)	2 months	Swedish public transportation employees	IES 39	43	21	NR	Medium
Nijdam et al., 2012[154]	BEP (70) EMDR (70)	17 weeks	Male and female Mixed	IES-R 72.8 to 79.9	38	56	100	Medium
Rothbaum et al., 1997[45]	EMDR (11) WL (10)	4 weeks (3 months)	Female Sexual assault	PSS-I 33.3 to 39.0	35	100	NR	Medium
Rothbaum et al., 2005[13]	PE (24) EMDR (26) WL (24)	4.5 weeks (6 months)	Female Sexual assault	Data reported in graphs only	34	100	32	Medium
Taylor et al., 2003[133]	PE (22) EMDR (19) Relaxation (19)	8 weeks (1 and 3 months)	Male and female Mixed	NR	37	75	23	Medium
ter Heide et al., 2016[43]	EMDR (37) Stabilization as usual (37)	9 sessions (2 weeks post, 3 months)	Refugees	75 to 78	40	27	NR	Low
van den Berg et al., 2015[16]	PE (53) EMDR (55) WL (47)	8 weeks (post, 6 months)	Psychotic disorders and PTSD Mixed	70	41	54	NR	Low
van der Kolk et al., 2007[47]	EMDR (29) Fluoxetine (30) Placebo (29)	8 weeks (6 months)	Male and female Mixed	71.2	36	83	33	Medium

[a]Data reported are mean or range of mean scores across groups for the PTSD measure listed.

BEP = brief eclectic psychotherapy; CAPS = Clinician-Administered Post Traumatic Stress Disorder Scale; CI = confidence interval; EMDR = eye movement desensitization and reprocessing; IES = Impact of Event Scale; IES-R = Impact of Event Scale-Revised; M-PTSD = Mississippi Scale for Combat-Related Post Traumatic Stress Disorder; N = total number randomized/assigned to intervention and control groups; NR = not reported; PE = prolong exposure; PSS-I = Post Traumatic Stress Disorder Symptom Scale-Interview; PTSD = posttraumatic stress disorder; TAU = treatment as usual; WL = wait-list; y = year.

trauma types.[16] Mean age was roughly similar across studies, ranging from 34 to 49 years. Four studies enrolled 70 percent or more female subjects.[13, 44, 45, 47] The primary outcome for the majority of studies was some version of the CAPS (CAPS, CAPS-2, or CAPS-Sx); two studies identified other primary outcomes, including the PSS-I[45] or IES.[44, 48]

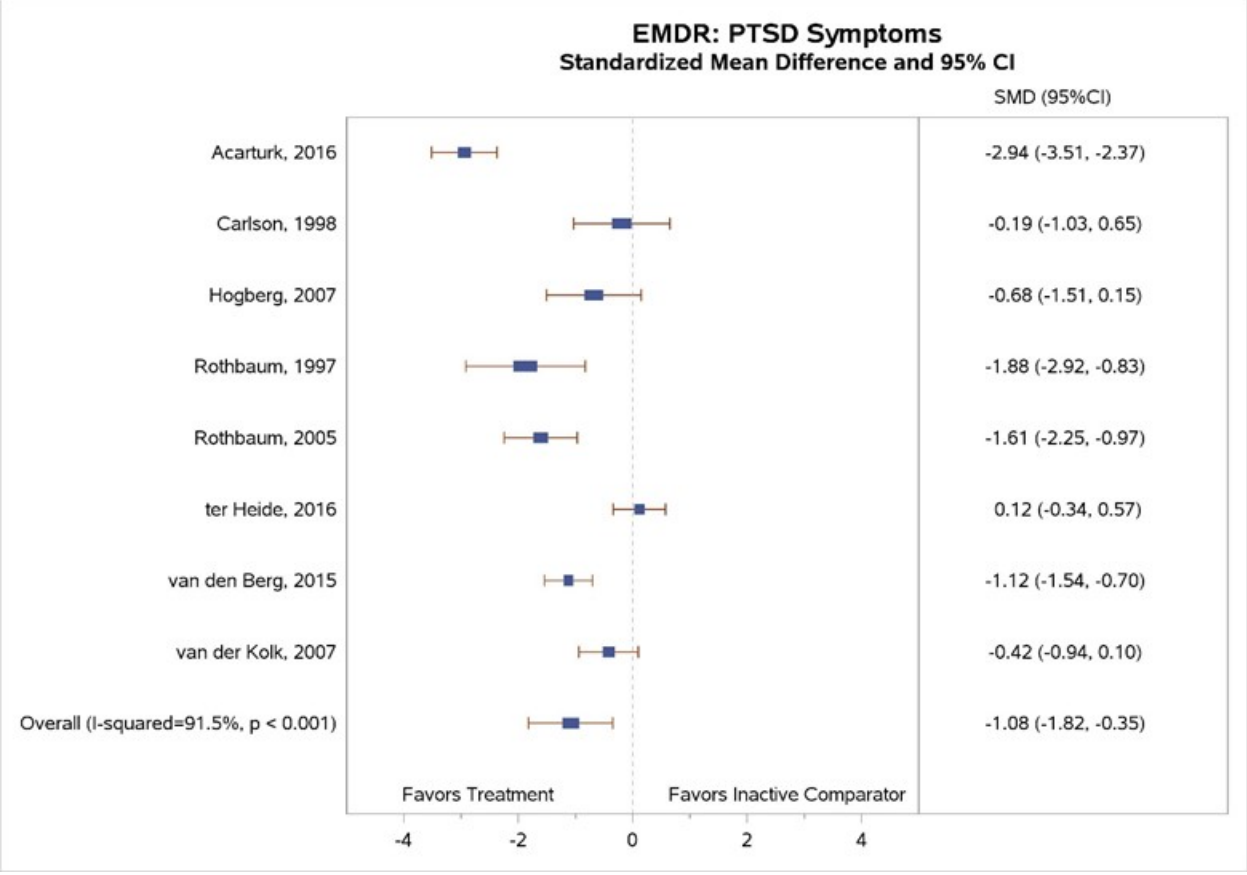
Among the studies with inactive comparators described above, two also included an active comparator arm of either PE[13] or relaxation.[46] Another study compared EMDR with either PE or relaxation therapy in a sample of individuals with PTSD with mixed trauma exposure types.[133] A fourth study included an active comparator (PE) and an inactive comparator (wait-list).[16]

Results for EMDR Compared With Inactive Comparators

PTSD Symptoms

All eight EMDR studies with inactive comparators measured PTSD symptom change. Our meta-analysis (Figure 13) found greater decreases in PTSD symptoms for EMDR than for inactive comparator subjects (SMD, -1.08; 95% CI, -1.82 to -0.35; I squared=91.5%, 8 studies; N=449).[13, 16, 43-48] Differences between EMDR and comparator groups reached statistical significance in four of eight studies;[13, 16, 44, 45] point estimates varied widely across studies (moderate SOE). The two studies that found a significant pre- to posttreatment benefit of EMDR and included followup assessments reported the maintenance of benefit at the 1-month[44] and 9-month[16] followup assessments.

Figure 13. Standardized mean change from baseline in PTSD symptoms for EMDR compared with inactive comparator



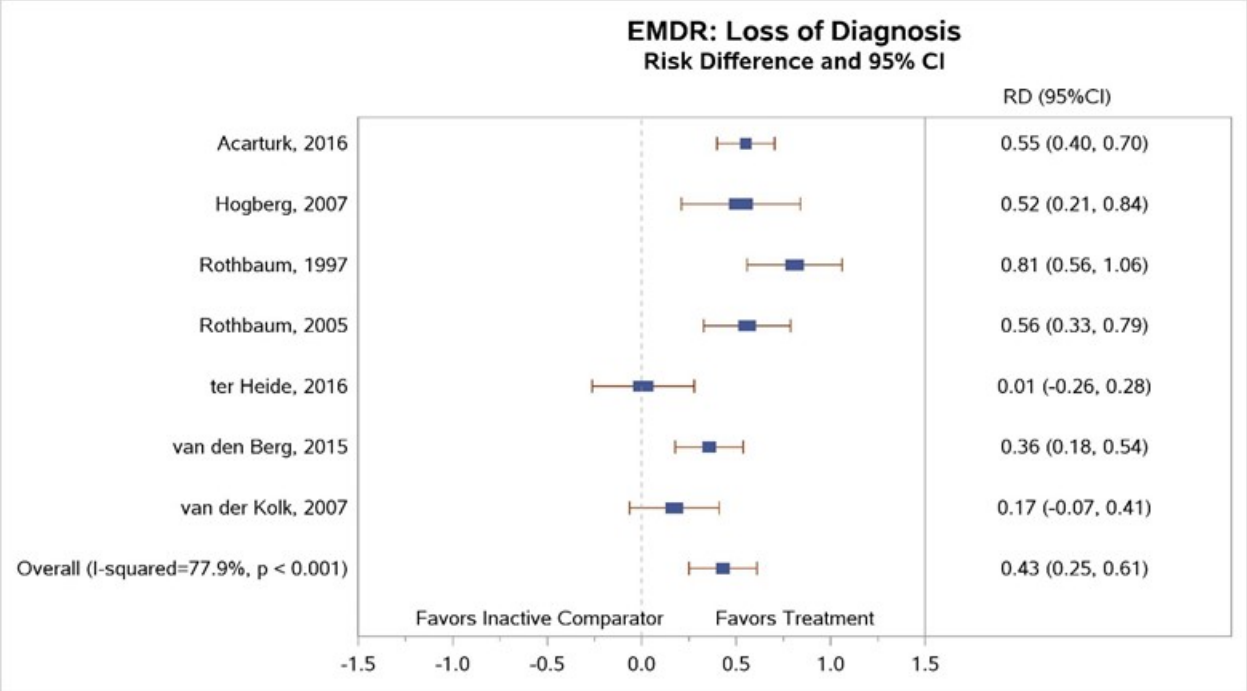
CI = confidence interval; EMDR = eye movement desensitization and reprocessing; PTSD = posttraumatic stress disorder; SMD = standardized mean difference.

Loss of PTSD Diagnosis

Of the studies that compared EMDR with inactive comparators, seven of the eight studies reported sufficient data to permit meta-analysis. Although one study that compared EMDR to stabilization as usual[43] did not find significant differences between groups, the other seven studies found a greater loss of diagnosis among EMDR subjects than inactive comparator subjects at posttreatment and at followup assessments.[13, 16, 44, 45, 47, 48] Our meta-analysis (Figure

14) found large between-group differences (RD, 0.43; 95% CI, 0.25 to 0.61) in loss of diagnosis at posttreatment assessment (moderate SOE).[47]

Figure 14. Loss of PTSD diagnosis for EMDR compared with inactive comparators



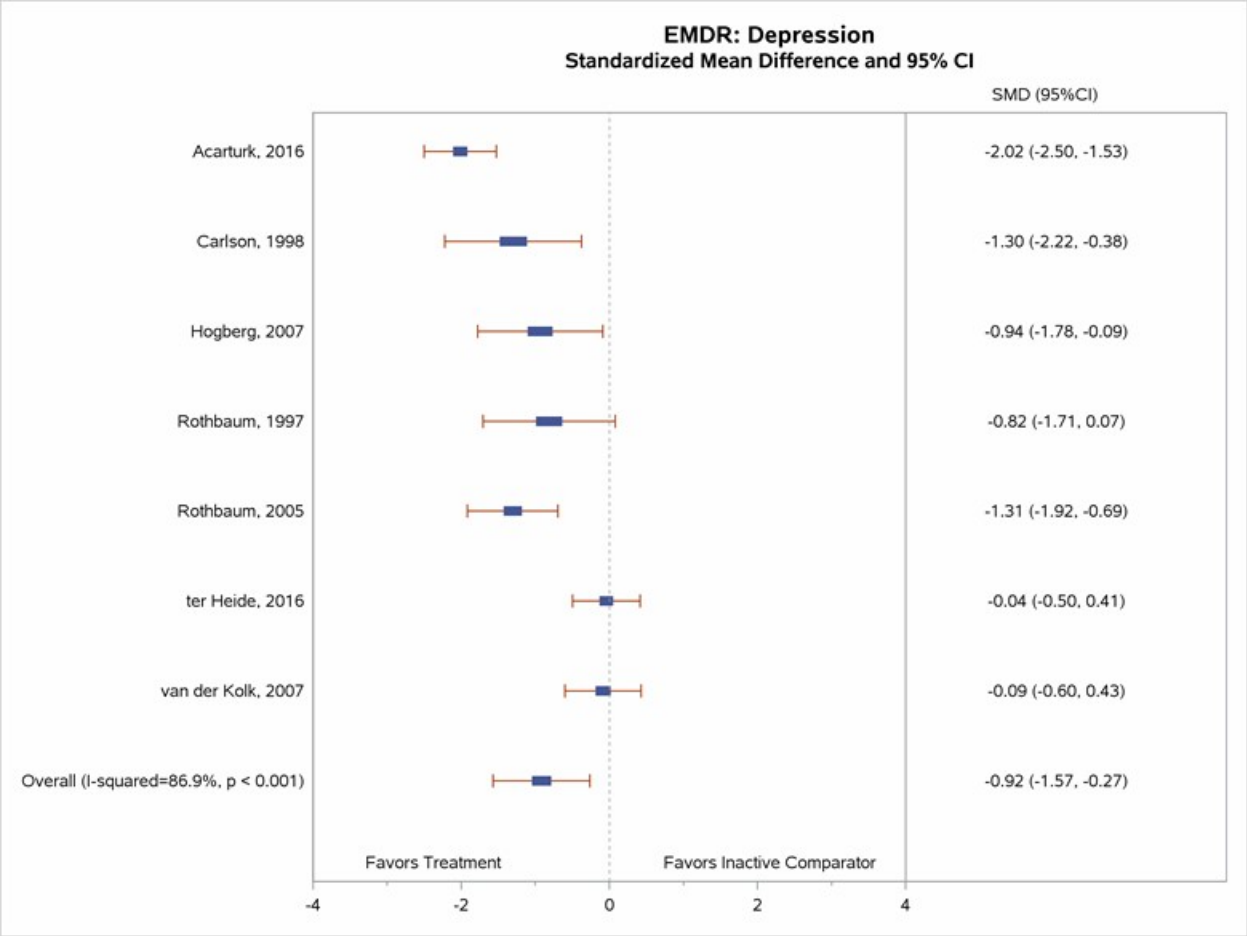
CI = confidence interval; EMDR = eye movement desensitization and reprocessing; RD = risk difference.

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Seven studies comparing EMDR with inactive comparators included a measure of depression symptoms (BDI, HAM-D, or Hopkins Symptom Check List [HSCL]-depression). All demonstrated better improvements in depression symptoms among EMDR group subjects, with four of the seven study comparisons reaching statistical significance.[13, 43, 44, 46, 48] Our meta-analysis (Figure 15) indicated a significant effect size (SMD, -0.91; 95% CI, -1.58 to -0.24; 7 studies; I squared=87.5%, N=347; moderate SOE).

Three studies used STAI,[13, 45, 46] and one used the anxiety subscale of the HSCL[43] to assess anxiety symptoms. Although all studies found that EMDR improved anxiety symptoms more than inactive controls, results did not reach statistical significance in three of the four studies (meta-analysis not conducted because of heterogeneity in sample characteristics, insufficient SOE).[13, 43, 45, 46]

Figure 15. Standardized mean change from baseline in depression symptoms for EMDR compared with control



CI = confidence interval; EMDR = eye movement desensitization and reprocessing; SMD = standardized mean difference.

Quality of Life

One study assessed quality-of-life outcomes.[43] Differences in quality-of-life changes from pre- to posttreatment did not significantly differ between the EMDR and stabilization-as-usual groups (insufficient SOE).

Results for EMDR Compared With Active Comparators: Relaxation

Of the studies comparing EMDR with an active comparator, three compared EMDR and exposure therapy;[13, 16, 133] as assessed in the CBT—Exposure section (above); one study compared EMDR with BEP[154] as assessed in the Other Psychological Intervention section (below). Two studies compared EMDR and relaxation.[46, 133]

PTSD Symptoms

One study found no statistically significant pre- to posttreatment difference in CAPS-assessed PTSD symptoms between subjects treated with EMDR and those treated with relaxation;[133] one found that EMDR led to greater PTSD symptom decreases than relaxation (N=13) on the Mississippi Scale for Combat Related PTSD but not on the IES (insufficient SOE).[46]

Loss of PTSD Diagnosis

Two studies that compared EMDR with relaxation both reported loss of PTSD diagnosis at some assessments.[46, 133] One reported loss of diagnosis at the end of treatment favoring EMDR over relaxation (RD, 0.20, p=ns), but differences did not reach statistical significance (insufficient SOE).[133]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Both studies used the BDI to measure depression symptoms; one also reported on anxiety symptoms using the STAI.[46] Neither study found a statistically significant difference between groups for reducing depression symptoms (insufficient SOE). One study reported a large between-group effect size (>0.90 using BDI) that was not statistically significant.[46, 133] The study that reported between-group differences of anxiety symptoms found that relaxation was less effective than EMDR (p<0.01) for reducing symptoms of anxiety at the end of treatment (insufficient SOE).[46]

Detailed Synthesis: Other Psychological Interventions

Characteristics of Studies

Table 15 summarizes the characteristics of 24 studies meeting our inclusion criteria. Further details describing the included studies are provided in Appendix D. For the characteristics and results sections included in this section, we group studies primarily by intervention type (rather than comparator) because of the large heterogeneity across studies.

Table 15. Characteristics of included studies of other psychological interventions

Study	Arm (N)	Treatment Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Boden et al., 2012[58]	SS (59) TAU (58)	12 weeks	Male Combat 92% of sample had clinical PTSD	IES-R 46.8 to 47.7	54	0	74	Medium
Church et al., 2013[155]	EFT (30) WL (29)	6 sessions (post/30 days, 3 months, 6 months)	U.S. combat Veterans	PCL-M 63.7	52	10	NR	Medium
Cook et al., 2010[156]	IRT (61) PsychEd (63)	6 weeks (1, 3, and 6 months)	Male Combat	79.5 to 81.3	59	0	58	Medium
Ford et al., 2011[59]	TAR (48) PCT (53) WL (45)	12 sessions[b] (3 and 6 months)	Female Victimization or incarceration 80% of sample had clinical PTSD	61.9 to 68.7	31	100	59	Medium
Ford et al., 2013[60]	TAR (41) SGT (39)	12 group sessions (post/ after treatment)	Incarcerated women victims of interpersonal violence 78% of sample had clinical PTSD	63 to 65	36	100	43	Medium

Study	Arm (N)	Treatment Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Gersons et al., 2000[51]	BEP (22) WL (20)	16 weeks (3 months)	Male and female police officers Trauma type NR	NR	37	12	NR	Medium
Hien et al., 2004[57]	Total 107[c] SS (unclear) RPC (unclear) UC (32)	12 weeks	Female Mixed w/substance abuse disorders 80% of sample had clinical PTSD	70.4 to 73.9	37	100	63	Medium
Hien et al., 2009[157] Hien et al., 2012[158]	SS (176) PsychEd[d] (177)	6 weeks	Female Mixed 88% of sample had clinical PTSD	61.6 to 64.2	39	100	54	Medium
Kearney et al., 2013[159]	MBSR+TAU (25) TAU (22)	8 weeks (post, 4 months)	War veterans Mixed	PCL 60 to 63	52	21	32	Medium
Krakow et al., 2001[52]	IRT (88) WL (80)	3 sessions—2 sessions 1 week apart and 1 session 3 weeks later (3 and 6 months)	Female Sexual abuse/assault	79.6 to 81.9	38	100	21	Medium
Langkaas et al., 2017[142]	PE (31) IRT (34)	10 weeks (post, 12 months)	Male and Female Mixed	PSS-I 33.2 to 34.9	45	58	NR	Medium
Lindauer et al., 2005[50]	BEP (12) WL (12)	16 weeks	Male and female Mixed	NR	39	54	NR	Medium
Markowitz et al., 2015[132] Markowitz et al., 2016[135]	PE (38) IPT (40) Relax (32)	14	Chronic PTSD	68.9 to 72.1	40	77	35	Medium
Maxwell et al., 2016[124]	MEST (8) CPT (8)	6 weeks (post, 3 months)	Male and female Mixed	MPSS-SR 54.13 to 63.50	NR	81	44	Medium
Moradi et al., 2014[160]	MEST (12) Control (12)	4 (post, 3 months)	Iranian Combat male veterans	NR	45	0	100	Medium
Morath et al., 2014[55]	NET (17) WL (17)	12 (4 months after treatment, 1-year followup)	Refugees and Asylum seekers	88	28	41	100	Medium
Neuner et al., 2004[161]	NET (17) Trauma couns (14) PsychEd (12)	3 to 4 weeks (4 and 12 months)	Male and female Sudanese refugees	PDS 19.5 to 25.2	33	61	100	Medium

Study	Arm (N)	Treatment Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Neuner et al., 2008[54]	NET (111) Trauma couns (111) MG (no intervention) (55)	3 weeks (6 months)	Male and female Rwandan and Somalian refugees	PDS 21.3 to 26.7	35	51	100	Medium
Neuner et al., 2010[53]	NET (16) TAU (16)	Weekly or biweekly sessions (median 9)[f]	Male and female Asylum seekers	PDS 36.9 to 38.9	31	31	NR	Medium
Nijdam et al., 2012[154]	BEP (70) EMDR (70)	16 weeks	Male and female Mixed	IES-R 72.8 to 79.9	38	56	100	Medium
Polusny et al., 2015[136]	MBSR (58) Group PCT (58)	8 weeks (post, 2 months)	War veterans Mixed	62	58	16	16	Medium
Schnyder et al., 2011[49]	BEP (16) MA (14)	16 weeks (6 months)[c]	Male and female Mixed 96% of sample had clinical PTSD	73.4 to 78.6	40	47	NR	Medium
van der Kolk et al., 2016[162]	Neurofeed-back training (28) WL (24)	12 weeks (post, 1 month)	Mixed	76 to 79	44	76	24	Medium
Zlotnick et al., 2009[56]	SS (27) TAU (22)	6 to 8 weeks (3 and 6 months)	Female Mixed 83% of sample had clinical PTSD	64.4 to 69.4	35	100	53	Medium

[a] Data reported are mean CAPS total or range of mean CAPS total scores across groups unless otherwise specified.
[b] Number of treatment sessions is reported when duration of treatment was not specified.
[c] The article did not report the numbers randomized to each group. It reported the numbers analyzed in each group (41, 34, and 32, respectively). It describes baseline data for 107 subjects analyzed. Of the 128 women who met full study eligibility criteria, 115 (90%) agreed to participate, and 96 of these women were randomly assigned to the two active treatment groups (SS and RPC). Thirty-two of the 128 women became the community care comparison group; they were not randomized to that group.
[d] Psycho Ed in this study is "Women's Health Education."
[e] Only the BEP group had a followup assessment; the control group did not.
[f] Treatment was terminated at the discretion of the therapist; range of 5 to 17 sessions provided.

Note: When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

BEP = brief eclectic psychotherapy; CAPS = Clinician-Administered PTSD Scale; EFT = emotional freedom techniques; F = female; IRT = imagery rehearsal therapy; MA = minimal attention (inactive control group); MBSR = mindfulness-based stress reduction; MEST = memory specificity training; MG = no-treatment monitoring group; MPSS-SR = Modified PTSD Symptom Scale-Self-Report; N = total number randomized/assigned to intervention and control groups; NET = narrative exposure therapy; NR = not reported; PCT = present-centered therapy; PDS = Posttraumatic Stress Diagnostic Scale; PE = prolonged exposure; PTSD = posttraumatic stress disorder; PsychEd = psychosocial education; RPC = relapse prevention condition; SGT = Supportive Group Therapy; SS = Seeking Safety; Ssm = sleep symptom monitoring; SUD = substance use disorder; TAR = Trauma Affect Regulation; TAU = treatment as usual; trauma couns = trauma counseling; UC = usual care; WL = wait-list; y = year.

Two studies assessed TAR (full intervention name: Trauma Affect Regulation: Guide for Education and Therapy). One study compared individually delivered TAR with two comparison groups (PCT and wait-list) in a population of mothers with victimization-related PTSD.[59] The

second study compared TAR delivered in a group setting with supportive group therapy in a population of incarcerated women victims of interpersonal violence.[60] Enrolled populations had a mean age of 31 to 36 years and had about half nonwhite participants (range 43% to 59%).

Four studies assessed BEP. Three of the four BEP studies had wait-list[50, 51] or minimal attention comparators;[49] one compared BEP with EMDR.[154] Three studies conducted by the same research group in the Netherlands had varying sample characteristics; one sampled police officers,[51] and the other two had heterogeneous subjects with a variety of index trauma types.[50, 154] Treatment lasted for 16 weeks in all four BEP studies, with similar mean age of participants across studies (35 to 40 years of age). Twelve subjects (40%) of the Swiss sample were taking psychotropic medications, "mostly antidepressants."

Three studies evaluated IRT.[52, 142, 156] One IRT study that tested efficacy versus wait-list involved women with a history of sexual trauma (N=168).[52] Another study compared IRT with psychoeducation in male Vietnam-era combat veterans with no medical disorders known to affect sleep (e.g., narcolepsy, untreated sleep apnea).[156] A third study tested the comparative effectiveness of IRT with PE among men and women with mixed trauma types. All studies included a 3-month followup posttreatment.

Four studies assessed the effectiveness of NET for PTSD among asylum seekers and refugees. Sample sizes ranged from 32 to 277. Duration of treatment ranged from 3 to 12 weeks. Three studies used the PDS to assess PTSD symptom severity, and one used the CAPS.[55] All samples contained males (25% to 69%) and females (31% to 75%) with mean ages ranging from 28 to 35 years. One study compared NET (n=17), SC (n=14), and psychoeducation (n=12) in a Ugandan refugee settlement with Sudanese refugees.[161] The second study, also conducted in a Ugandan refugee settlement, compared NET (n=111), trauma counseling (n=111), and a nontreatment symptom monitoring group (n=55) among Rwandan and Somalian refugees.[54] The third study compared NET (n=16) with treatment as usual (n=16) in a sample of asylum seekers living in Germany who were originally from Turkey, the Balkans, or Africa.[53] The fourth study compared NET (n=17) with a wait-list control (n=17) in a sample of refugees and asylum seekers from Africa and the Middle East who were living in Switzerland.[55]

Two studies tested MEST. One enrolled Iranian combat male veterans and compared outcomes against those who received a control treatment[160] while the other tested the comparative effectiveness of MEST and CPT among men and women with mixed trauma types.[124] Both included followup assessments 3 months postintervention.

Two studies tested MBSR in samples of male and female war veterans. One tested MBSR plus treatment as usual (TAU) versus TAU,[159] and the other tested MBSR versus an active control, group PCT.[136] MBSR is a treatment that uses meditation to increase awareness of present mental and physical processes. In MBSR, the instructor leads participants through meditative exercises that focus on noticing sensations, thoughts, and emotions without judgment, and the participants practice short guided meditation exercises outside of group sessions. Three studies assessed other (unique) psychological interventions including the following: IPT,[132] EFT,[155] and neurofeedback training.[162] Appendix A details characteristics of each of these treatments. The study assessing IPT had two active comparator groups: PE and relaxation therapy.[132] The other two studies compared an intervention with an inactive control. The enrolled population in each study had different trauma types (Table 15).

Four studies assessed the efficacy of SS; three different active control approaches contained components to treat SUDs alone or to provide psychoeducation about women's health issues.[56, 57, 157] One of these three studies compared the addition (to TAU) of a voluntary SS intervention

with a treatment-as-usual control group, which comprised incarcerated women enrolled in a residential substance use treatment program in a minimum security wing.[56] Another active control involved TAU in a SUD clinic at a Veteran's Administration outpatient mental health clinic.[58] Three of the studies enrolled women generally in their 30s; one enrolled male veterans with a mean age of 54.[58] Sample sizes ranged from 49 to 353;[56, 57, 157] one of these was a pilot study (N=49) that may have been underpowered.[56] One study enrolled a sample of incarcerated women;[56] two enrolled community-based samples of women seeking substance abuse treatment.[57, 157] Followup assessments were conducted at 3 and 6 months in all studies; one study each conducted additional assessments at 9 months[57] or 12 months.[157]

Trauma Affect Regulation

PTSD Symptoms

Two studies assessing TAR in populations of women with interpersonal victimization reported between-group changes in CAPS scores (low SOE). The study that compared TAR, PCT, and wait-list reported greater improvement in CAPS-assessed PTSD symptoms for those treated with TAR than those in the wait-list group (between-group mean difference, -17.4; $p<0.001$).[59] The study that compared TAR with usual group care for incarcerated women found a similar reduction in CAPS-assessed PTSD symptoms between groups (between-group mean difference, -2.7; p=NS).[60]

Remission

Both studies reported on the percentage of participants with full remission from baseline to followup with inconsistent findings. One study found a higher rate of remission among the TAR group than among the wait-list group (RD, 0.21; $p<0.001$);[59] the other found a lower rate of remission among the TAR group than among the usual-care group (RD, -0.11; insufficient SOE).[60]

Loss of Diagnosis

Both studies reported on loss of PTSD diagnosis from baseline to followup; one found a higher rate of remission in the TAR group than in the wait-list group (RD, 0.26), and the other found a similar rate of remission in both groups (RD, 0.01; p=NR; insufficient SOE).[60]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

The study that compared TAR with a wait-list control reported greater decreases in depression symptoms and anxiety symptoms for the TAR than for the wait-list group (BDI between-group mean difference, -4.1; $p<0.01$; STAI between-group mean difference, -6.3; p=0.19; insufficient SOE).

Brief Eclectic Psychotherapy

PTSD Symptoms

Two studies reported measures of PTSD symptoms for BEP compared with an inactive comparator.[49, 50] One only reported subscale scores, however, for the Structured Interview for PTSD (SI-PTSD) measure between groups.[50] The study that used CAPS reported significantly

greater decreases in PTSD symptoms in the BEP versus the wait-list group (between-group mean difference=-10.8; 1 study; N=30; insufficient SOE).[49, 51]

The study that compared PTSD symptoms between BEP and EMDR groups reported that both treatments were equally effective in reducing PTSD symptom severity, but EMDR resulted in faster recovery.[154] The study reported significant decreases in PTSD symptoms within both treatment groups using the IES-R and the SI-PTSD but greater decreases from baseline to the first assessment for those treated with EMDR than for those treated with BEP (between-group mean difference on SI-PTSD -10.80; 95% CI, -15.23 to -6.37).[154] The between-group difference did not remain significant at the second assessment, conducted after both groups had completed treatment (insufficient SOE).

Remission

One study (N=30) reported data on symptom remission. At the end of treatment, a greater proportion of BEP than inactive comparator group subjects had remitted (RD 0.13) as defined by having a CAPS score of less than 20.[49] Difference persisted at the 6-month followup (RD 0.19). None of the subjects in the wait-list group achieved complete remission at either assessment (insufficient SOE).

Loss of PTSD Diagnosis

All three BEP studies reported efficacy for loss of PTSD diagnosis at the end of treatment and followup assessments using different assessment measures. The RDs ranged from 0.13 to 0.58 in individual studies.[49-51] We concluded that evidence supports the efficacy of BEP for loss of PTSD diagnosis (low SOE).

The study that compared BEP with EMDR reported similar rates at the end of treatment (RD=0.08 slightly favoring EMDR), but EMDR subjects had quicker time to loss of PTSD diagnosis than BEP subjects (RD at mid-treatment 0.40 favoring EMDR; insufficient SOE).[154]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

All three studies comparing BEP with wait-list reported on reduction of depression and anxiety symptoms. Two used the Hospital Anxiety and Depression Scale (HADS) as an outcome measure; both studies reported that BEP subjects had significantly greater decreases in depression symptoms at the end of treatment and followup than wait-list subjects and at later followup (low SOE).[49, 50] One study used the Symptom Checklist-90 (SCL-90) as a multidimensional indicator of psychopathology and reported that BEP had greater decreases in depression symptoms than wait-list at the end of treatment (data not reported, $p<0.01$) that persisted at the 3-month followup.[51]

Two studies reported that BEP had significantly greater decreases in anxiety symptoms (low SOE) as assessed by the HADS (Cohen's $d=0.8$, $p<0.05$ and $d=0.9$, $p<0.05$ for one study at the end of treatment and at followup;[49] for the other study $d=0.54$[50]). The study using the SCL-90 reported that BEP had greater decreases in anxiety symptoms at the end of treatment and at the 3-month followup (data not reported, p-values of <0.05 and <0.01).[51]

The study comparing BEP with EMDR reported measures of depression and anxiety symptoms (using the HADS depression and the HADS anxiety).[154] Similar to findings for other outcomes (e.g., PTSD symptoms), the study reported greater improvement from baseline to the first assessment for those treated with EMDR than for those treated with BEP but no significant

difference between groups at the second assessment (insufficient SOE, see Appendix F for detailed data).

Return to Work or Active Duty

Two studies reported outcomes related to work (insufficient SOE)—one reported the percentage of subjects on sick leave;[50] the other reported the percentage who had returned to work.[51] The former study found fewer subjects on sick leave for the BEP group compared with those on the wait-list, but the difference was not statistically significant (d=0.33, p=0.06).[50] The second study reported significantly greater rates of returning to work among BEP subjects than those in the inactive comparator group (RD 0.26; p<0.05) for return to work.[51]

Imagery Rehearsal Therapy

PTSD Symptoms

One IRT study found efficacy for decreases in CAPS-assessed PTSD symptoms among IRT-treated versus wait-list control groups (between-group mean difference, -21.0; p=0.001; low SOE).[52]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

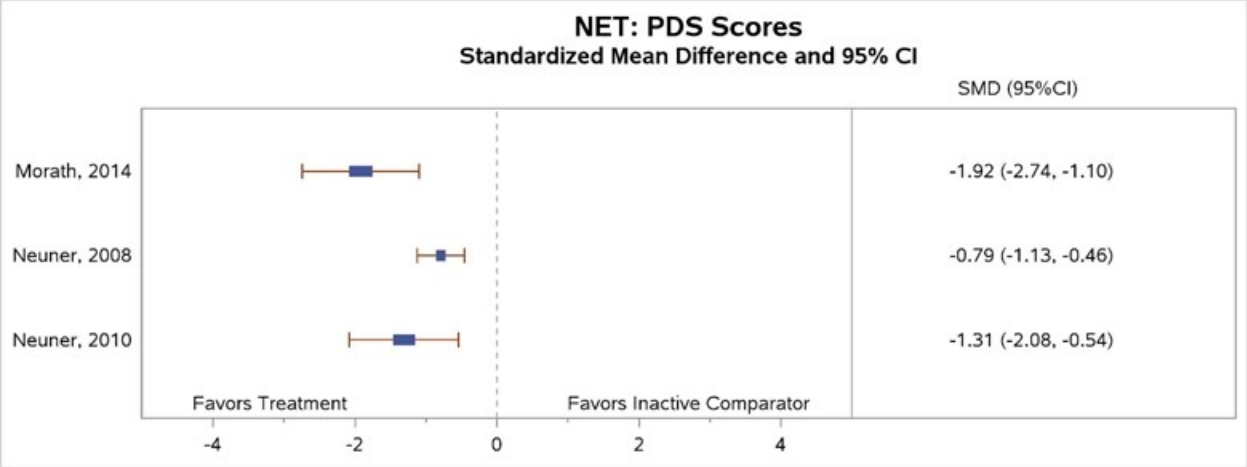
One study that assessed the efficacy of IRT on depressive symptoms using the HAM-D found greater, but not significantly different, decreases in depression among IRT participants compared with wait-list participants (insufficient SOE).[52] This study also found significant (p<0.04) differences in changes in anxiety symptoms between groups at the end of treatment, but differences resulted from the IRT group having decreases in symptoms and the wait-list group having increases in symptoms.

Narrative Exposure Therapy

PTSD Symptoms

All three studies that compared NET with an inactive comparator found that NET subjects had greater decreases in PTSD symptoms at the end of treatment (moderate SOE; Figure 16).[53-55] One study reported a reduction (but no data) in PTSD symptoms for subjects in the intervention group at the followup assessment 6 months after the end of treatment;[53] another reported that the intervention led to significantly greater decreases in PTSD symptoms than no treatment (i.e., monitoring group) from baseline to the 6-month followup (d=1.4 and 0.08, respectively, p<0.001).[54]

Figure 16. Standardized mean change from baseline to end of treatment in PTSD symptoms for narrative exposure therapy compared with inactive controls

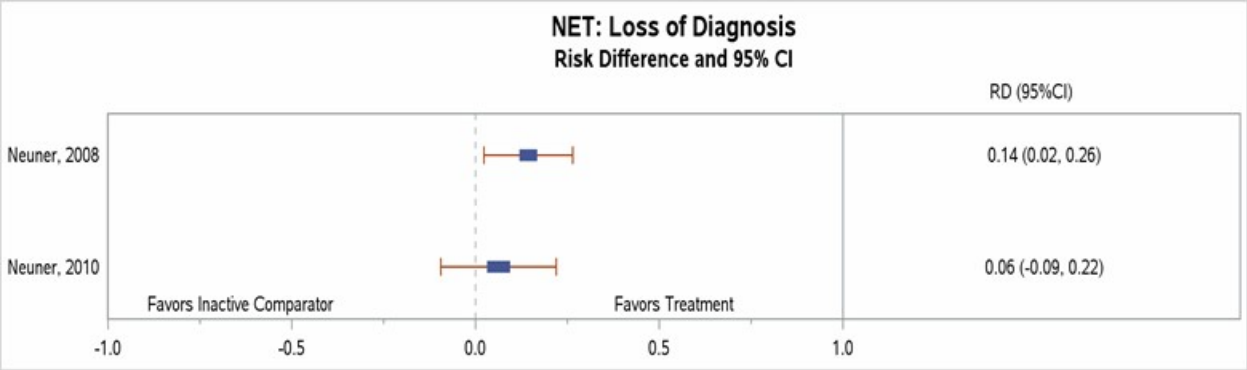


CI = confidence interval; NET = narrative exposure therapy; PDS = Posttraumatic Diagnostic Scale; SMD = standardized mean difference.

Loss of PTSD Diagnosis

Two studies of NET and an inactive control reported data on loss of PTSD diagnosis (low SOE; Figure 17).[53, 54] One of these studies also had an active comparator group (trauma counseling), for which we did not intend to assess comparative effectiveness.[54] Both studies with inactive comparators favored NET for loss of PTSD diagnosis at the end of treatment (RD of 0.06 and 0.14 in the two studies).[54, 161]

Figure 17. Loss of PTSD diagnosis for narrative exposure therapy compared with inactive controls



CI = confidence interval; NET = narrative exposure therapy; RD = risk difference.

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Two studies evaluated the efficacy of NET on coexisting psychiatric conditions.[53, 55] Both studies that compared NET with an inactive control reported greater decreases in depressive symptoms for NET subjects compared with inactive comparator subjects at the end of treatment; however, only one comparison likely attained statistical significance (Cohens d=0.54 but p=NR; insufficient SOE).[53, 55, 161]

One small study (N=32) found greater decreases on Composite International Diagnostic Interview-Pain scores for NET versus inactive comparator subjects at the end of treatment (insufficient SOE).[53]

Interpersonal Therapy

One study compared IPT with two active comparators, PE and relaxation, in a population with PTSD primarily related to interpersonal trauma.[132] The prior CBT-Exposure section, above, details the comparative effectiveness of PE versus relaxation and PE versus IPT. In this section, we focus on the comparative effectiveness of IPT versus relaxation only.

PTSD Symptoms

Participants randomized to IPT therapy had a similar decrease in PTSD symptom scores as assessed by the CAPS compared with the relaxation therapy group (between-group mean difference, -6.3 favoring IPT; p=0.097).[132] On the PSS, however, participants in the IPT group had greater decreases in scores than the relaxation group (between-group mean difference, -18.2 favoring IPT; p=0.008; insufficient SOE).[132]

Remission

The study that compared IPT versus relaxation found similar rates of PTSD remission (defined as CAPS score <20) across groups (RD 0.04 favoring IPT; insufficient SOE).[132]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

The comparative effectiveness of IPT and relaxation for change in depression symptoms as assessed by the HAM-D did not differ at the end of treatment (between-group mean difference, -0.3; insufficient SOE).[132]

Quality of Life

IPT subjects had greater increases in quality-of-life ratings as assessed by the Quality of Life Enjoyment and Satisfaction Questionnaire[163] than the relaxation therapy group (between-group mean difference, 10.1 favoring IPT; p<0.001; insufficient SOE).[132]

Functional Impairment

IPT subjects had greater increases in interpersonal functioning as measured by the Inventory of Interpersonal Problems than those in the relaxation group (between-group mean difference, -0.46 favoring IPT; p=0.001; insufficient SOE).[132]

Memory Specificity Training

PTSD Symptoms

One study enrolling Iranian combat veterans compared MEST with a no treatment control group; participants in the MEST group had significantly fewer PTSD symptoms on the IES-R than the control group at followup (insufficient SOE).[160]

The MEST comparative effectiveness study found that reductions in PTSD symptoms were not similar and not statistically different among subjects randomized to the MEST group and the CPT group. The MEST group participants experienced similar decreases in symptoms after attending only about half of the sessions attended by the CPT group participants (insufficient SOE).[124]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

The study reported no significant difference between participants in the MEST group and controls[160] or MEST versus CPT[124] on depression symptoms measured by the BDI-II (scores not reported; insufficient SOE for both efficacy and comparative effectiveness).

Mindfulness-Based Stress Reduction

Of the two MBSR studies that met review inclusion criteria, this section describes the findings for the study that tested the efficacy of MBSR plus TAU versus TAU.[159] The other study tested MBSR versus an active comparison group for which we were not interested in comparative effectiveness (group PCT).[136] One study compared IPT with two active comparators, PE and relaxation, in a population with PTSD primarily related to interpersonal trauma.[132] The prior CBT-Exposure section above details the comparative effectiveness of PE versus relaxation and PE versus IPT. In this section, we focus on the comparative effectiveness of IPT versus relaxation only.

PTSD Symptoms

No significant differences were found between reduction in PTSD symptoms at posttreatment between those in the MBSR+TAU group versus the TAU group (insufficient SOE).[159]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Differences in posttreatment decreases in depressive symptoms as measured by the Patient Health Questionnaire (PHQ-9) were not significantly significant across treatment groups (MBSR+TAU versus TAU; insufficient SOE).[132]

Neurofeedback

The single neurofeedback (NF) study that met review inclusion criteria tested NF training versus a wait-list comparison group.[162]

PTSD Symptoms

The NF group had significantly greater decreases in PTSD as measured by the CAPS (between-group mean difference, -26.8, $p<0.05$) and by the Davidson Trauma Scale (DTS) (mean=-20.7, $p<0.05$) than the wait-list group at the posttreatment assessment (insufficient SOE).[162] Between-group differences were sustained at the 1-month followup assessment.

Loss of PTSD Diagnosis

In the single small study that met review inclusion criteria, loss of diagnosis comparisons favored the NF group over the wait-list group (RD, 0.40, $p=0.0002$; insufficient SOE).[162]

Emotional Freedom Techniques

PTSD Symptoms

One study enrolling U.S. veterans compared EFT with wait-list control; participants in the EFT group had a greater decrease in PTSD symptoms measured by the PCL-M than controls at the end of treatment assessment (between-group mean difference, -22.1; $p<0.0001$; insufficient SOE).[155]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

A single study found significantly greater decreases in psychiatric symptoms at the end of treatment for EFT than inactive comparator subjects for both domains tested from the Symptom Assessment-45 Questionnaire (insufficient SOE).[155]

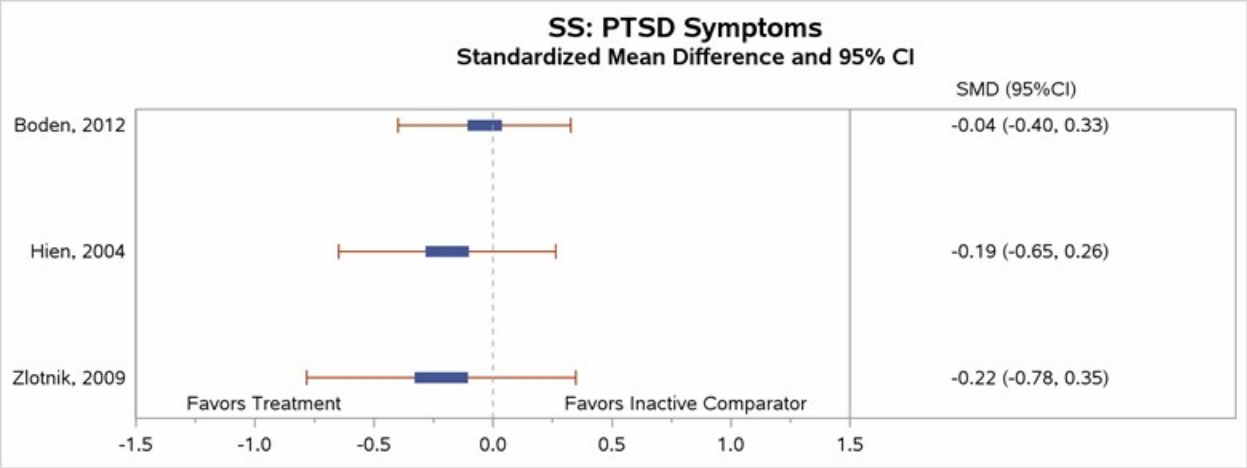
Seeking Safety

PTSD Symptoms

Four studies tested the efficacy or effectiveness of SS.[56-58, 157] Three compared SS with usual care,[56-58] and two compared SS with an active comparator, but not ones for which we sought to determine comparative effectiveness (i.e., psychoeducation,[157] relapse prevention[57]).

The three studies comparing SS with usual care each found that the intervention participants had greater decreases in PTSD symptoms than usual-care participants; however, between-group differences did not reach statistical significance (meta-analysis not performed because of heterogeneity in sample and study characteristics, low SOE for no difference).[56-58] Figure 18 shows the SMD and CIs for between-group differences in PTSD symptoms.

Figure 18. Mean change from baseline in PTSD symptoms for Seeking Safety compared with inactive comparator



CI = confidence interval; PTSD = posttraumatic stress disorder; SMD = standardized mean difference; SS = Seeking Safety.

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Analyses of data from two[57] studies compared substance use outcomes between SS and usual-care subjects. At the end of treatment, one study found no between-group differences for abstinence and substance use severity at the end of treatment,[56] and the other study found significantly greater decreases in drug use (but not alcohol use) among SS subjects compared with usual-care subjects at the end of treatment assessment (insufficient SOE).[58]

KQ 1a. Variability in Efficacy or Comparative Effectiveness of Psychological Interventions by Patient Characteristics or Type of Trauma

This subquestion of KQ 1 evaluated whether the efficacy or comparative effectiveness of any of the psychological interventions differed by patient characteristics or type of trauma

experienced. To answer this question, we present findings from included studies that reported outcomes for subgroups of interest (defined by patient or trauma factors) and compare the efficacy or comparative effectiveness across subgroups. Four studies provided information about efficacy or comparative effectiveness across different subgroups of interest.

Key Points

- Three studies compared the efficacy and one study examined the comparative effectiveness of interventions across subgroups of participants defined by patient characteristics or type of trauma experienced.
- These studies compared subjects with child- versus adult-onset sexual abuse (CPT vs. wait-list and PE vs. wait-list), child- versus adult-onset traumatic event exposure (EMDR vs. placebo), borderline personality disorder versus without borderline personality disorder (DBT vs. usual-care wait-list), and comparative effectiveness between subjects with versus without major depressive disorder (PE vs. IPT vs. relaxation).
- Insufficient SOE exists to determine the efficacy or comparative effectiveness between subgroups.

Detailed Synthesis: Patient Characteristics or Trauma Type

Characteristics of Included Studies

Table 16 summarizes the characteristics of the five included studies (2 of which examined different moderators of the same trial). Each study included a subgroup analyses of trials that have been described in previous parts of this report. Each examined a different treatment comparison, although three studies (2 of which examined different moderators of the same trial) included PE as one of the treatment arms.[3, 132, 135] Only one of the four studies (2 moderator studies from the single trial) did not include a followup after posttreatment assessment.[132, 135] All used the CAPS as the primary outcome measure. Additional details describing the included studies can be found in Appendix F.

One study examined the efficacy and comparative effectiveness of CPT and PE (versus a wait-list comparator) within a sample of female rape survivors enrolled in a clinical trial (n=171)[3] who also had childhood sexual abuse (n=121).[125] The second study compared EMDR, fluoxetine, and placebo in subjects with a variety of trauma types including child sexual abuse, child physical abuse, child sexual and physical abuse, adult sexual assault, adult physical assault, domestic violence, other adult victimization, traumatic loss, war/terror/violence, and injury/accident.[47] The authors reported subgroup analyses for those with child-onset trauma and those with adult-onset trauma. The third study that included subgroup comparisons tested the efficacy of DBT against a wait-list, treatment-as-usual group of child abuse survivors.[23] The efficacy of DBT was compared between those with and without borderline personality disorder. The fourth and fifth studies, which tested moderators from the same trial, examined the comparative effectiveness of PE, IPT, and relaxation training among a group of adults with chronic PTSD of mixed trauma types.[132, 135] Subgroup analyses compared the effectiveness of different treatments among adults with and without major depressive disorder, trauma type, gender, and age of primary trauma exposure.

Table 16. Characteristics of included studies that compared efficacy or comparative effectiveness between patients having different characteristics or specific trauma types

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Bohus et al., 2013[23]	DBT (43) TAU-WL (39)	24 weeks (post, 6 weeks, 12 weeks)	Child abuse survivors Subgroup analysis: BPD	83 to 88	36	100	NR	Medium
Markowitz et al., 2015[132, 135]	PE (38) IPT (40) Relaxation (32)	14	Chronic PTSD Mixed Subgroup analysis: MDD, trauma type, gender, age of primary trauma exposure	68.9 to 72.1	40	77	35	Medium
Resick et al., 2002[3] Resick, et al., 2003[125]	CPT (62) PE (62) WL (47)	6 weeks (3 and 9 months)	Female Sexual assault Subgroup analysis: history of child sexual abuse	69.9 to 76.6	32	100	29	Medium
van der Kolk et al., 2007[47]	EMDR (29) Fluoxetine (30) Placebo (29)	8 weeks (6 months)	Male and female Mixed subgroup analysis: child-onset and adult-onset trauma	71.2	36	83	33	Medium

[a] Data reported are mean CAPS totals or range of mean CAPS total scores across groups unless otherwise specified.
BPD = borderline personality disorder; CAPS = Clinician-Administered PTSD Scale; DBT = dialectical behavior therapy; CPT = cognitive processing therapy; EMDR = eye movement desensitization and reprocessing; F = female; IPT = interpersonal therapy; MDD = major depressive disorder; N = total number randomized/assigned to intervention and control groups; PE = prolonged exposure; PTSD = posttraumatic stress disorder; TAU = trauma affect regulation; WL = wait-list; y = year.

Efficacy or Comparative Effectiveness by Patient Characteristic or Trauma Type

Each of the five studies examined a different patient characteristic or trauma type and treatment comparison (insufficient SOE for each analysis). The study that compared the efficacy and comparative effectiveness of CPT, PE, and wait-list) between women rape victims with versus without childhood sexual abuse found similar efficacy of CPT and PE across both subgroups (those with versus without childhood sexual abuse).[125]

The second study that compared the efficacy and comparative effectiveness of EMDR, fluoxetine, and placebo between those with childhood-onset (prior to age 18) versus adult-onset trauma[47] found no significant differences in the efficacy of EMDR as compared with placebo by trauma onset (child vs. adult) as tested by interaction analysis. Interestingly, however, in the main effects analysis, adults with childhood-onset PTSD had worse outcomes than those with adult-onset PTSD, regardless of what intervention they received.

The third study that reported on whether the efficacy of DBT (as compared with a wait-list usual-care comparison group) varied between women with childhood sexual abuse-related PTSD with versus without borderline personality disorder[23] found no differences in efficacy across subgroups. DBT appeared to have similar efficacy, regardless of the presence of comorbid borderline personality disorder.

The fourth and fifth studies examined whether the comparative effectiveness of PE, IPT, and relaxation therapy differed among those with versus without comorbid major depressive disorder,[132] and trauma type (sexual, physical, or interpersonal), gender, and age of primary trauma exposure (18 years old or younger versus 19 years old or older).[135] In the first study, the authors reported no significant subgroup differences in PTSD symptom changes at posttreatment in the comparative effectiveness of any of the treatments tested; the effect of the treatment

response (CAPS score at posttreatment <20) between groups did not significantly differ at posttreatment. The authors reported that among subjects in the PE treatment group, those with comorbid major depressive disorder had significantly higher attrition rates than those without major depressive disorder (50% vs. 5.6%, respectively, $p<0.05$).[132] In the second moderator study, whereas those without sexual trauma exposure had no differences in efficacy across treatment groups, those with sexual trauma exposure had greater efficacy with IPT as compared with PE or relaxation training ($p<0.05$). Gender and age of primary trauma exposure, however, did not moderate the efficacy findings.

KQ 2. Efficacy and Comparative Effectiveness of Different Pharmacological Treatments

To answer this question, we present findings from placebo-controlled efficacy trials (indirect evidence) followed by evidence from head-to-head trials (direct evidence) to assess the comparative effectiveness of pharmacotherapies rated as having low or medium risk of bias. We used meta-analyses to pool data when five or more studies (or 3 or more studies with low heterogeneity across studies) tested similar interventions and reported similar outcome data; when three or four studies that tested a single intervention were determined to have substantial heterogeneity in sample, intervention, or study characteristics or two or fewer studies testing the same intervention presented data for an outcome, we qualitatively synthesized the findings and present findings from the individual studies. We also conducted network meta-analysis to use both the indirect and direct evidence to determine the comparative effectiveness of pharmacotherapies. We detail the comparative effectiveness of interventions that demonstrated efficacy of at least moderate SOE. In the bulleted text below, we summarize the main overall key points and then the key points for each medication class and report the SOE where appropriate.

We used the same set of outcomes of interest described previously in the chapter focused on psychological interventions (KQ 1). In brief, the primary outcomes of interest that investigators used to determine the effectiveness of treatments for adults with PTSD include PTSD symptoms, loss of PTSD diagnosis, and symptom remission, as defined by study authors based on loss of symptoms below a predefined threshold level. We also comment on other outcomes of interest, such as prevention or reduction of coexisting medical or psychiatric conditions (especially depression, anxiety, and substance use problems). As in the KQ 1 section above, for continuous outcomes such as PTSD, depression, and anxiety symptoms or ratings of quality of life or functioning, we present the between-group mean difference for single studies or the SMD when describing more than one study to indicate the between-group difference in pre- to posttreatment or pre- to followup assessments. For dichotomous outcomes like remission and loss of PTSD diagnosis, we report the RD between groups.

For outcomes with evidence from three or more studies with low heterogeneity across trials or five or more studies testing the same intervention types, we present the pooled estimate from meta-analysis and the 95 percent CI. When three or four studies determined to have substantial heterogeneity in sample, intervention, or study characteristics or two or fewer studies testing the same intervention present data for an outcome, we qualitatively synthesized the findings and present findings from the individual studies.

All included studies are cited in the detailed synthesis section and related tables and figures presented in this section for each treatment. Section headings within each detailed synthesis section include each outcome reported by at least one included study of that treatment type. If an

outcome does not appear in the section, no included study testing the intervention of interest reported data on it.

Appendices contain additional information about the risk of bias assessments (Appendix E), individual study characteristics and findings for each outcome presented in evidence tables (Appendix F), characteristics and consistency of findings of high risk of bias studies not synthesized in the text (Appendix G), forest plots depicting individual and pooled study findings (Appendix H), and detailed information about each component contributing to the SOE grade (Appendix I).

Key Points: Overall—Efficacy of Pharmacological Treatments

- For PTSD symptom reduction, fluoxetine (selective serotonin reuptake inhibitor [SSRI]), paroxetine (SSRI), and venlafaxine (serotonin and norepinephrine reuptake inhibitor [SNRI]) have evidence of efficacy (moderate SOE). Low SOE supports the efficacy of prazosin (alpha blocker), topiramate (anticonvulsant), olanzapine and risperidone (atypical antipsychotics), and sertraline (SSRI).
- For PTSD symptom remission, paroxetine (SSRI) and venlafaxine (SNRI) have evidence of efficacy (moderate SOE).

Table 17 summarizes the efficacy and SOE for all included medications for primary outcomes of interest, PTSD symptoms, remission, and loss of PTSD diagnosis, although no drug efficacy studies included loss of PTSD diagnosis as an outcome measure.

Table 17. Summary of efficacy and strength of evidence of PTSD pharmacological treatments

Treatment		N Trials (Subjects)	Findings	SOE
Fluoxetine (SSRI)	PTSD symptoms[a]	4 (835)[47, 61-63]	Reduced PTSD symptoms SMD -0.28 (95% CI -0.42 to -0.14)	Moderate
	Depression symptoms[b]	3 (771)[47, 61, 62]	Similar reduction in depression symptoms SMD -0.20 (95% CI -0.40 to 0.00)	Low SOE for no difference[c]
Paroxetine (SSRI)	PTSD symptoms[a]	2 (348)[64, 65]	Reduced PTSD symptoms SMD of -0.56 to -0.44 in individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
	PTSD symptom remission	2 (348)[64, 65]	Greater PTSD symptom reduction RD of 0.13 and 0.19 across 2 individual studies (1 of 2 studies p<0.05)	Moderate
	Depression symptoms[b]	2 (348)[64, 65]	Reduced depression symptoms SMD range -0.60 to -0.34 across individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate

Treatment		N Trials (Subjects)	Findings	SOE
Sertraline (SSRI)	PTSD symptoms[a]	7 (1,085)[66-72]	Reduced PTSD symptoms SMD -0.20 (95% CI -0.36 to -0.04)	Low[d]
	Depression symptoms[b]	7 (1,085)[66-72]	Similar reduction in depression symptoms SMD -0.14 (95% CI -0.33 to 0.06)	Low for no difference[e]
Venlafaxine (SNRI)	PTSD symptoms[a]	2 (687)[69, 73]	Reduced PTSD symptoms SMD -0.35 and -0.26 across two individual studies	Moderate
	PTSD symptom remission	2 (687)[69, 73]	Greater PTSD symptom remission RD of 0.12 and 0.15 across individual studies	Moderate[f]
	Depression symptoms[b]	2 (687)[69, 73]	Reduced depression symptoms Between-group mean difference of -2.6 and -1.6 across individual studies	Moderate[g]
Prazosin (alpha blocker)	PTSD symptoms[a]	3 (117)[74-76]	Reduced PTSD symptoms SMD -0.52 (95% CI, -0.90 to -0.14)	Low
Topiramate (anticonvulsant)	PTSD symptoms[a]	3 (142)[77-79]	Reduced PTSD symptoms SMD range of -1.85 to -0.38 across individual studies	Low[h]
Olanzapine (antipsychotic)	PTSD symptoms[a]		Reduced PTSD symptoms	Low
		2 (47)[80, 81]	SMD of -1.15 and -0.96 across individual studies,[80, 81] both significantly favored treatment	
		3 (62)[80-82]	SMD range -1.15 to 0.89 across individual studies	
			All studies favored treatment (2 of 3 studies p<0.05)	
Risperidone (antipsychotic)	PTSD symptoms[a]	4 (422)[83-86]	Reduced PTSD symptoms SMD -0.26 (95% CI, -0.52 to -0.01)	Low

NOTE: Outcomes graded as insufficient are not included in this table. Insufficient evidence was provided for divalproex (anticonvulsant), tiagabine (anticonvulsant), citalopram (SSRI), all TCAs, buproprion (other second-generation antidepressant [SGA]), and mirtazapine (other SGA). No studies that met inclusion criteria rated as having low or medium risk of bias evaluated lamotrigine (anticonvulsant), any benzodiazepine, desvenlafaxine (SNRI), duloxetine (SNRI), nefazodone (other SGA), or trazodone (other SGA).

[a] SMD from Clinician-Administered PTSD Scale and other various PTSD symptom scales.
[b] SMD from the Beck Depression Inventory and other various depression symptom scales.
[c] SOE changed from moderate in the prior review to low for no difference in the updated review. Only 2 of 3 studies favored treatment; one favored placebo. Imprecision, inconsistency, and effect sizes near the null prompted the change in grade.

[d] SOE changed from moderate in the prior review to low in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, and findings were imprecise.
[e] SOE changed from low to low for no difference in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, findings were imprecise, and most individual study estimates were close to the null.
[f] SOE changed from insufficient to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
[g] SOE changed from low to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
[h] SOE changed from moderate in the prior review to low in the updated review. The findings were imprecise; only 1 of 3 individual studies found significant differences between study groups, and the sample sizes were small.

CI = confidence interval; N = number; PTSD = posttraumatic stress disorder; RD = risk difference; SGA = second-generation antidepressant; SMD = standardized mean difference; SNRI = serotonin and norepinephrine reuptake inhibitor; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

Key Points: Overall—Comparative Effectiveness of Pharmacological Treatments

- Very few head-to-head trials were identified.
  - Two studies provided moderate SOE for no differences between venlafaxine and sertraline for depression symptom reduction and low SOE provided no difference for PTSD symptoms reduction, quality of life, and disability.
  - Our network meta-analysis of 33 trials (4,817 subjects) that included CAPS-measured PTSD symptom outcomes found no significant differences between the three pharmacological treatments that had at least moderate SOE of efficacy: fluoxetine, paroxetine, and venlafaxine.

Key Points: Alpha Blockers

- Low SOE supports the efficacy of prazosin on PTSD symptoms reduction.

Key Points: Anticonvulsants

- Low SOE supports the efficacy of topiramate on PTSD symptoms reduction.

Key Points: Atypical Antipsychotics

- Low SOE supports the efficacy of olanzapine and risperidone on PTSD symptoms reduction.
- Low SOE supports the efficacy of risperidone on anxiety symptoms reduction.

Key Points: Selective Serotonin Reuptake Inhibitors

- Moderate SOE supports the efficacy of fluoxetine for PTSD symptoms and low SOE for the anxiety symptoms. Low SOE does not support the efficacy of fluoxetine for depressive symptoms.
- Moderate SOE supports the efficacy of paroxetine for PTSD symptoms, remission, depression symptoms, and disability.
- Low SOE supports the efficacy of sertraline for PTSD symptoms reduction and quality of life (low SOE) and supports no differences in efficacy between sertraline and placebo for depression symptoms.

- Moderate SOE supports no differences in effectiveness between venlafaxine and sertraline for depression and low SOE supports no difference in effectiveness for PTSD symptom reduction, quality of life, and disability.

Key Points: Serotonin and Norepinephrine Reuptake Inhibitors

- Moderate SOE supports the efficacy of venlafaxine for PTSD symptoms, remission, depression symptoms, quality of life, and disability/functional impairment
- Moderate SOE supports no differences in effectiveness between venlafaxine and sertraline for depression and low SOE supports no difference in effectiveness for PTSD symptoms, quality of life, and disability (low SOE for no differences).

Detailed Synthesis: Placebo-Controlled Trials of Alpha-Blockers

Characteristics of Studies

We found three studies meeting our inclusion criteria that studied the efficacy of alpha-blockers (Table 18), each testing the efficacy of prazosin. All enrolled subjects had moderate to severe PTSD. All studies enrolled all or a large majority of male subjects; average age ranged from 30 to 56 years. Trial durations ranged from 8 weeks[75] to 20 weeks.[74, 75] Further details describing the included studies are provided in Appendix F.

Table 18. Characteristics of included placebo-controlled trials of alpha-blockers

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Raskind et al., 2003[74]	Prazosin 2 to 10 mg (5) Placebo (5)	20	Male Combat veterans	79.1 to 83.6	53	0	NR	Medium
Raskind et al., 2007[75]	Prazosin 2 to 15 mg (20) Placebo (20)	8	Male and female Combat veterans	70.0	56	5	35	Medium
Raskind et al., 2013[76]	Prazosin 1 mg titrated to a max of 20 mg for men or 10 mg for women (32) Placebo (35)	15	Veterans Active-duty soldiers, Combat trauma	77.3 to 85.7	30	15	37	Medium

[a] Data reported are mean CAPS or range of mean CAPS scores across groups unless otherwise specified.
Note: When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

CAPS = Clinician-Administered PTSD Scale; F = female; mg = milligram; N = total number randomized/assigned to intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; y = year.

Results for Placebo-Controlled Trials of Alpha-Blockers

PTSD Symptoms

All three studies reported greater pre- to posttreatment decreases in CAPS-assessed PTSD symptoms for subjects treated with prazosin than for those receiving placebo (SMD, -0.52, 95% CI, -0.90 to -0.14. I squared=0.0%, 3 studies, N=117; low SOE; Appendix H).[74-76]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

One of the included studies assessed depression using the HAM-D.[75] The study found that patients treated with prazosin had greater decreases in depression symptoms than those administered placebo, but differences between groups failed to reach statistical significance (between-group mean difference, -5.0; p=0.08; insufficient SOE).

Detailed Synthesis: Placebo-Controlled Trials of Anticonvulsants/Mood Stabilizers

Characteristics of Studies

Table 19 summarizes the six studies that met inclusion criteria. Appendix F contains further details about each study. The studies enrolled subjects with moderate to severe PTSD. Sample sizes ranged from 28 to 232. Treatment duration ranged from 8 to 12 weeks. Three of the included studies focus on combat-related PTSD;[77, 164, 165] three enrolled a heterogeneous group of subjects with a variety of index trauma types (e.g., physical and sexual assault/violence, witnessing harm or death, combat, natural disaster, childhood sexual abuse, childhood physical abuse, MVA).[78, 79, 166] The studies generally recruited middle-aged adults, with mean ages ranging from ~40 to ~55 years. Three studies enrolled at least two-thirds female subjects;[78, 79, 166] three enrolled all or nearly all males. Five studies used some version of the CAPS as the primary outcome; one assessed PTSD symptoms using the PCL.[165]

Table 19. Characteristics of included placebo-controlled trials of anticonvulsants, by drug

Study	Arm (Dose mg/Day) (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Akuchekian et al., 2004[77]	Topiramate (12.5 to 500) (34) Placebo (33)	12	Male Combat veterans	49.8	40	0	100	Medium
Batki et al., 2014[165]	Topiramate (25 to 300) (14) Placebo (16)	12	Veterans w/ AUD, warzone and/or civilian related trauma	72.8 to 83.1	50	7	7	Low
Davidson et al., 2007[166]	Tiagabine (4 to 16) (116) Placebo (116)	12	Male and female Mixed	82.6	423	66	NR	Medium
Davis et al., 2008[164]	Divalproex (1,000 to 3,000) (44) Placebo (41)	8	Male and female Combat veterans	75.2 to 77.3	55	2	NR	Low
Tucker et al., 2007[78]	Topiramate (25 to 400) (20) Placebo (20)	12	Male and female Mixed	88.3 to 91.1	41	79	11	Medium
Yeh et al., 2011[79]	Topiramate (25 to 200) (17) Placebo (18)	12	Male and female Mixed	66.1 to 78.8	40	68	NR	Medium

[a] Data reported are mean CAPS or range of mean CAPS scores across groups unless otherwise specified.

AUD = alcohol use disorder; CAPS = Clinician-Administered PTSD Scale; F = female; mg = milligram; N = total number randomized/assigned to intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; y = year.

Results of Placebo-Controlled Trials of Anticonvulsants/Mood Stabilizers

PTSD Symptoms

Five of the included studies reported CAPS-assessed PTSD symptom changes between groups (Appendix H). Among the three topiramate studies, only one found significant differences across groups,[77] although all effect sizes consistently favored topiramate (Figure 19; low SOE).[78, 79]

One study testing divalproex and another testing tiagabine[166] provided insufficient evidence of efficacy for PTSD symptoms due to unknown consistency and imprecise findings.

Remission

Two anticonvulsant study reported between-group differences in remission: one trial of tiagabine[166] and one of topiramate.[78] Both study defined remission as having a CAPS score of less than 20 at the end of treatment. Neither study found a statistically significant difference between anticonvulsants and placebo (insufficient SOE for tiagabine and for topiramate due to unknown consistency and imprecise findings).

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Three studies, one that assessed divalproex[164] and two that tested topiramate,[78, 79] reported between-group changes in depression symptoms (Appendix F). None of the studies reported statistically significant between-group decreases in depression symptoms from pre- to posttreatment, although all point estimates favored anticonvulsants (insufficient SOE).[78, 79, 164]

Two studies (one divalproex and the other topiramate) reported between-group differences in anxiety symptoms assessed by the Hamilton Anxiety Scale (HAM-A). Neither study found statistically significant reductions in anxiety between groups (see Appendix F; insufficient SOE).[78, 164]

Disability or Functional Impairment

Two studies, one of tiagabine and one of topiramate, reported between-group differences in disability assessed by the Sheehan Disability Scale (SDS).[78, 166] Both studies reported similar changes between subjects treated with medication and those treated with placebo (see Appendix F for details; insufficient SOE).

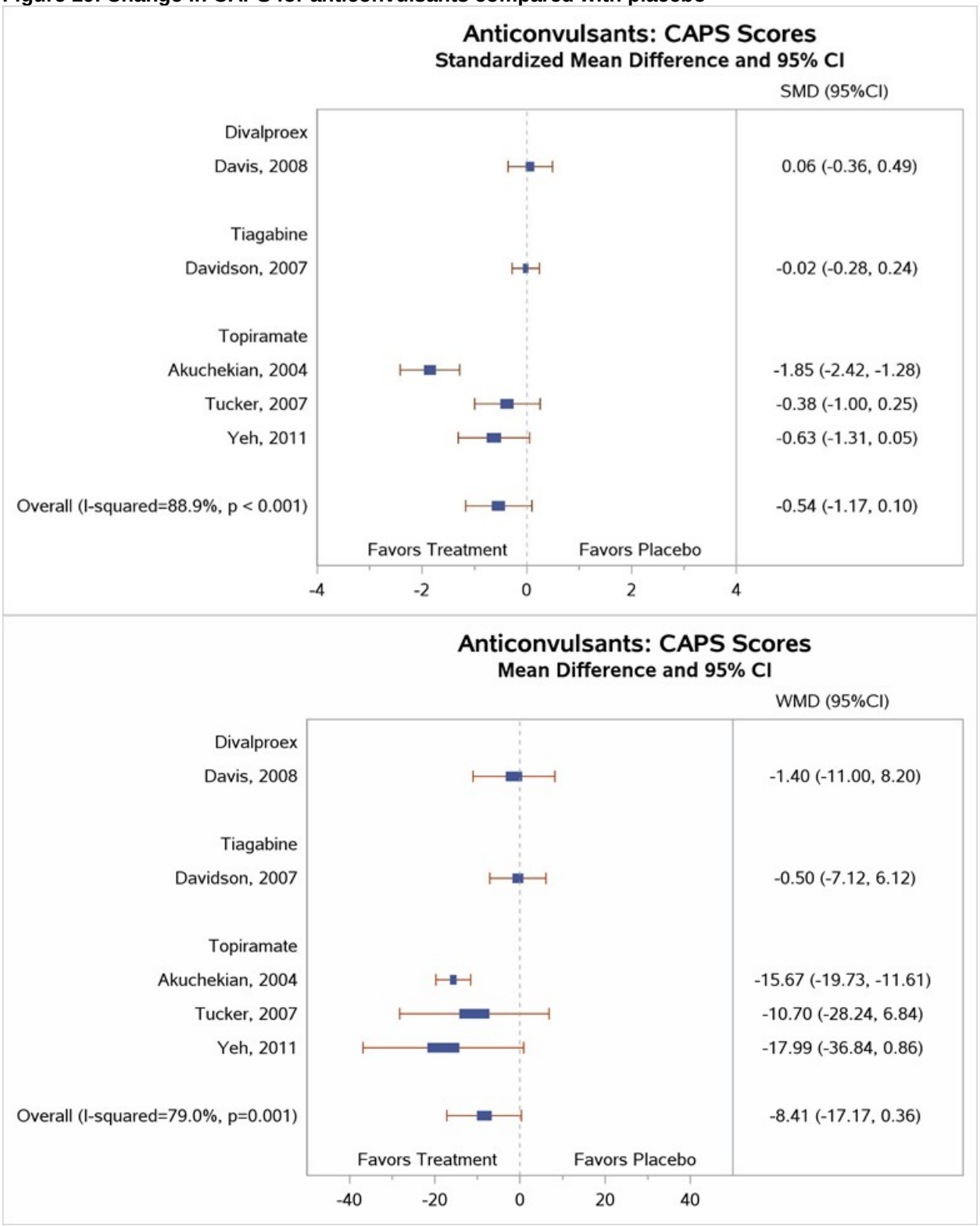
Detailed Synthesis: Placebo-Controlled Trials of Atypical Antipsychotics

Characteristics of Studies

Figure 20 summarizes the characteristics of the eight studies meeting our inclusion criteria. Appendix F provides details to further describe the studies included in this section.

Evidence of the efficacy of atypical antipsychotics comes from five studies that compared risperidone with placebo and three studies that compared olanzapine with placebo. Relatively small samples (ranging from 15 to 65) tested drug interventions that lasted from 5 weeks to 6 months. Subjects had mean ages generally ranging from 41 to 54. Although two studies enrolled a majority[82] or only[84] females, three enrolled exclusively males.[80, 83, 86, 167]

Figure 19. Change in CAPS for anticonvulsants compared with placebo



CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; SMD = standardized mean difference; WMD = weighted mean difference.

Table 20. Characteristics of included placebo-controlled trials of atypical antipsychotics, by drug

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% F	% Non-white	Risk of Bias
Bartzokis et al., 2005[86]	Risperidone 1 to 3 mg (33) Placebo (32)	16	Male Combat veterans	98.6 to 102.2	52	0	32	Medium
Butterfield et al., 2001[82]	Olanzapine 5 to 20 mg (10) Placebo (5)	10	Male and female Mixed	SIP 39.7 to 45.9	43	93	46	Medium
Carey et al., 2012[81]	Olanzapine 5 to 10 mg (14) Placebo (14)	8	Adults w/non-combat related chronic PTSD, Noncombat	79.4 to 81.6	41	61	NR	Medium
Hamner et al., 2003[83]	Risperidone 1 to 6 mg (20) Placebo (20)	5	Male Combat veterans	89.1 to 90.3	52	0	54	Medium
Krystal et al., 2011[85]	Risperidone 1 to 4 mg (147) Placebo (149)	24	Male and female Combat	78.2	54	3	34	Low
Monnelly et al., 2003[167]	Risperidone 0.5 to 2 mg (8) Placebo (8)	6	Male Combat veterans	PCL-M 72 to 73	51	0	20	Medium
Reich et al., 2004[84]	Risperidone 0.5 to 8 mg (12) Placebo (9)	8	Female Childhood abuse	65.5 to 73.9	28	100	14	Medium
Stein et al., 2002[80]	Olanzapine 10 to 20 mg (10) Placebo (9)	8	Male Combat veterans	84.0 to 86.1	52	0	NR	Medium

[a] Data reported are mean CAPS or range of mean CAPS scores across groups unless otherwise specified.
Note: When mean data for baseline PTSD severity, sex, or race were not reported for the total sample but were presented for each study arm, we provide the range across arms.

CAPS = Clinician-Administered PTSD Scale; F = female; mg = milligram; N = total number randomized/assigned to intervention and control groups; NR = not reported; PCL-M = PTSD Checklist – Military Version; PTSD = posttraumatic stress disorder; SIP = Structured Interview for PTSD; y = year.

Most studies enrolled subjects with trauma types ranging from combat-related trauma,[80, 83, 85, 86, 167] childhood abuse-related trauma,[84] mixed types of trauma,[82] to other types of trauma not related to combat.[81, 168] One study exclusively enrolled subjects with PTSD and concurrent psychotic features,[83] although studies frequently excluded subjects with a history of comorbid schizophrenia, bipolar disorder, or recent substance abuse/dependence.[81-84, 167]

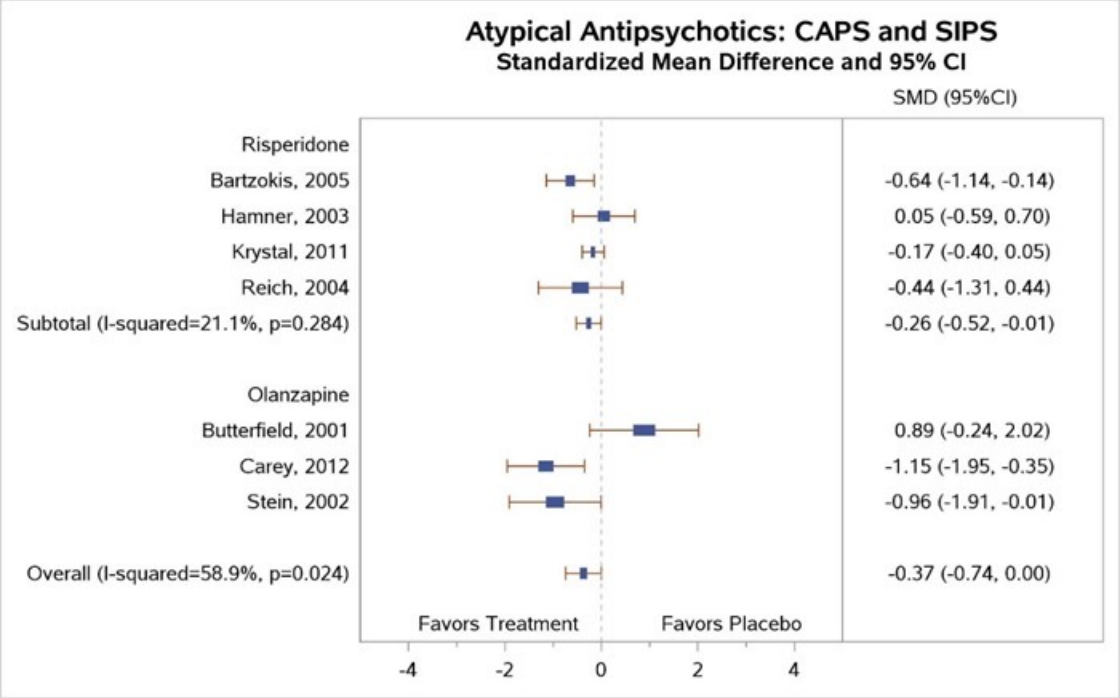
The majority of studies permitted cointerventions. Most studies assessed PTSD symptoms using some version of the CAPS (CAPS total, CAPS-1, CAPS-2);[80-86] one used the PCL-M to compare between-group outcomes.[167]

Results of Placebo-Controlled Trials of Atypical Antipsychotics

PTSD Symptoms

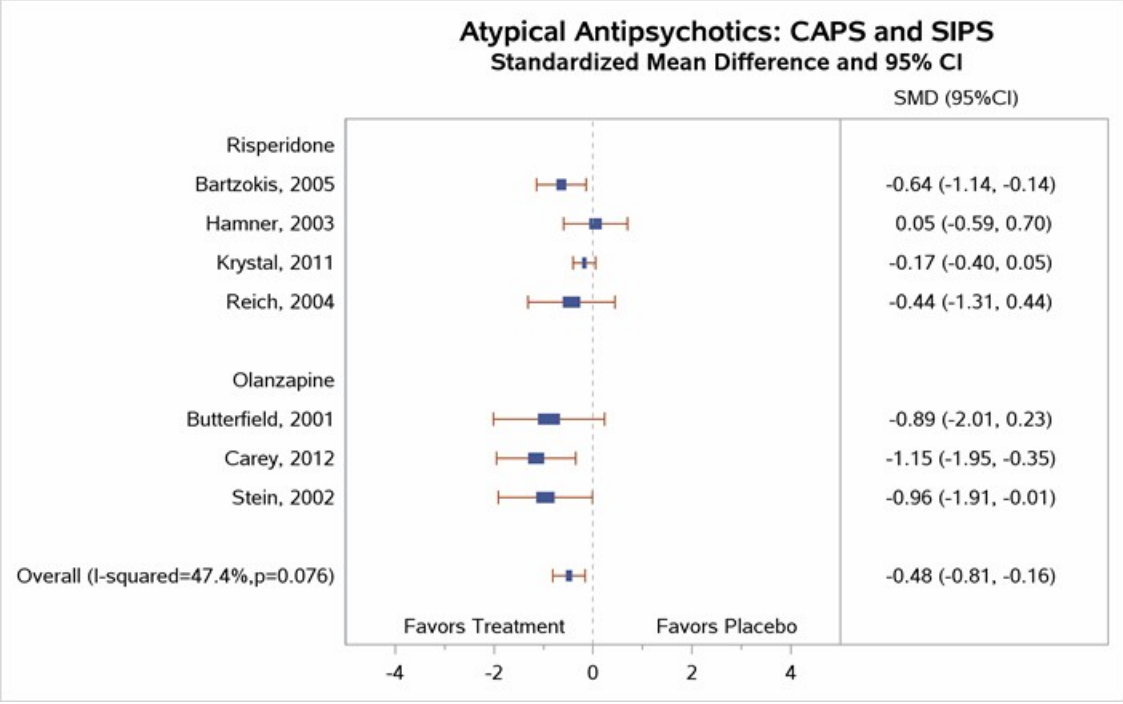
Three studies compared PTSD symptoms between olanzapine and placebo (low SOE). Two studies demonstrated efficacy for CAPS-measured PTSD symptoms (Figure 20).[80, 81] Another study[82] that did not use CAPS to assess PTSD symptoms but instead used four other measures of PTSD symptoms, including Single Item PTSD Screeners (SIPS), also favored olanzapine, but differences in this very small study did not reach statistical significance (see Figure 21).

Figure 20. Change in CAPS for atypical antipsychotics compared with placebo



CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; PTSD = posttraumatic stress disorder; SIPS = Single Item PTSD Screener; SMD = standardized mean difference.

Figure 21. Change in PTSD symptoms for atypical antipsychotics compared with placebo



CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; SMD = standardized mean difference; SIPS = Single Item PTSD Screener.

For risperidone, four studies compared CAPS-assessed PTSD symptoms between treatment and placebo subjects and found some evidence of efficacy (SMD, -0.26, 95% CI, -0.52 to -0.01; I

squared=21.1%; 4 studies; N=422; Figure 20; low SOE). One study found no real differences between groups,[83] two suggested benefit but found no significant differences in PTSD symptoms between risperidone and placebo,[84, 85] and one study found modest but very imprecise evidence of risperidone benefit.[86]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Two very small studies found slight benefits of varying levels of statistical significance favoring olanzapine for depression symptoms as measured by the Center for Epidemiologic Studies Depression Scale (between-group mean difference, -0.37; N=19; $p<0.03$)[80] and the Montgomery Åsberg Depression rating scale (between-group mean difference , -0.54; N=28; $p=0.14$; insufficient SOE).[81]

For risperidone compared with placebo, one study indicated nonsignificant benefit of risperidone over placebo for HAM-D-measured depression symptoms (between-group mean difference, -2.3; N=65; $p>0.05$) and significant efficacy of risperidone over placebo for HAM-D-measured anxiety symptoms (between-group mean difference, -5.4; N=65; $p<0.001$).[86] Another small study that enrolled subjects experiencing symptoms of psychosis at enrollment reported a greater reduction in Positive and Negative Syndrome Scale–measured psychotic symptoms at the end of treatment among risperidone than placebo subjects (between-group mean difference, -7.7, N=40; $p<0.05$; low SOE).[83]

Disability or Functional Impairment

Two very small studies found conflicting evidence of the efficacy of olanzapine on SDS-measured disability compared with placebo (between-group mean difference, 0.3 in 1 study and -4.2 in another, with a combined N of 43; insufficient SOE).

Detailed Synthesis: Placebo-Controlled Trials of Benzodiazepines

We found no studies with low or medium risk of bias meeting our inclusion criteria.[169]

Detailed Synthesis: Selective Serotonin Reuptake Inhibitors

Characteristics of StudiesTable 21 summarizes the characteristics of the 17 studies meeting our inclusion criteria. Further details describing the studies are provided in Appendix F.

Table 21. Characteristics of included placebo-controlled trials of selective serotonin reuptake inhibitors, by drug

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Brady et al., 2000[66]	Sertraline 25 to 200 mg (94) Placebo (93)	12	Male and female Mixed	75.1 to 76.6	40	73	16	Medium
Brady et al., 2005[67]	Sertraline 150 mg (49) Placebo (45)	12	Male and female Mixed, alcohol dependence	57.6 to 60.1	37	46	NR	Medium
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171]	Fluoxetine 10 to 60 mg (27) Placebo (27)	12	Male and female Mixed	DTS 73.7 to 79.4	37	91	7	Medium

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Davidson et al., 2006[69]	Total 538[b] Venlafaxine 37.5 to 375 mg (179) Sertraline 25 to 200mg (173) Placebo (179)	12	Male and female Mixed	~82	NR	NR	NR	Medium
Davidson et al.,2001[68]	Sertraline 25 to 200 mg (100) Placebo (108)	12	Male and female Mixed	73.5 to 73.9	37	78	17	Medium
Friedman et al., 2007 [70]	Sertraline 25 to 200 mg (86) Placebo (83)	12	Male and female Mixed (71% combat)	72.1 to 73.8	46	20	71	Medium
Li et al., 2017[172]	Sertraline 135 mg (36) Placebo (36)	12	Male and female Mixed	IES-R 63.9 to 64.8	46	12	100	Low
Marshall et al., 2001[64]	Paroxetine 20 mg (188) Paroxetine 40 mg (187) Placebo (188)	12	Male and female Mixed	74.3 to 75.3	42	NR (~2:1 F:M)	<10%	Medium
Martenyi et al., 2002[61]; Martenyi et al., 2006[173]	Fluoxetine 20 to 80 mg (226) Placebo (75)	12	Male and female Combat and victim/witness of war	80.5 to 81.3	38	19	9	Medium
Martenyi et al., 2007[62]	Fluoxetine 20 mg (163) Fluoxetine 40 mg (160) Placebo (88)	12	Male and female Mixed	75 to 79	41	72	23	Medium
Panahi et al., 2011[71]	Sertraline 50 to 200 mg (35) Placebo (35)	10	Male Combat	IES-R 65.1 to 65.4	46	0	100	Low
Simon et al., 2008[174]	Paroxetine 12.5 to 62.5 mg (11) Placebo (14)	10	Male and female Mixed (60% exposure to war; combat % NR), refractory to exposure	SPRINT 16.1 to 17	46	56	26	Medium
Tucker et al., 2001[65]	Paroxetine 20 to 50 mg (163) Placebo (160)	12	Male and female Mixed	73.2 to 74.3	41	66	28	Medium
Tucker et al., 2003[175] Tucker et al., 2004[176]	Citalopram 20 to 50 mg (25) Sertraline 50 to 200 mg (23) Placebo (10)	10	Male and female Mixed	83.9 to 94.2	39	74	14	Medium
van der Kolk et al., 1994[63]	Fluoxetine 20 to 60 mg (33) Placebo (31)	5	Male and female Mixed (48% combat)	NR	40	34	NR	Medium
van der Kolk et al., 2007[47]	Fluoxetine (30) EMDR (29) Placebo (29)	8[c]	Male and female Mixed	71.2	36	83	33	Medium
Zohar et al., 2002[72]	Sertraline 50 to 200 mg (23) Placebo (19)	10	Male and female Israeli military veterans	91.2 to 93.3	40	12	NR	Medium

[a] Data reported are mean CAPS or range of mean CAPS scores across groups unless otherwise specified.
[b] The Ns for each are the number analyzed; the number randomized to each group was not reported (overall N was 538; 531 were included in the analysis).
[c] Study was 8 weeks of treatment but also included a 6-month posttreatment followup.

CAPS = Clinician-Administered PTSD Scale; DTS = Davidson Trauma Scale; EMDR = eye movement desensitization and reprocessing; F = female; IES-R = Impact of Event Scale-Revised; mg = milligram; N = total number randomized/assigned to

intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; SPRINT = Short PTSD Rating Interview; y = year.

Sample sizes ranging from 12 to 563 tested SSRI efficacy over a duration of 5 to 12 weeks of treatment. The mean age of subjects in the samples spanned from 36 to 46 years; females comprised the majority of samples in 9 of 16 studies.[47, 62, 64-66, 68, 170, 175, 177] The primary outcome for the majority of studies included some version of the CAPS (CAPS, CAPS-2, or CAPS-Sx); 5 studies identified other primary outcomes, including Treatment Outcome PTSD Scale,[61, 62] DTS,[178] Duke Global Rating for PTSD,[170] IES,[71, 172] or Short PTSD Rating Interview (SPRINT).[174]

Results of Placebo-Controlled Trials of Selective Serotonin Reuptake Inhibitors

PTSD Symptoms

Our meta-analyses found that subjects who received paroxetine, fluoxetine, and sertraline (but not citalopram) had significantly greater decreases in CAPS-assessed PTSD symptoms than subjects who received placebo (Figure 22). The single citalopram study indicated greater decreases in PTSD symptoms among placebo subjects than citalopram subjects, although differences did not reach statistical significance (insufficient SOE). Each of the four fluoxetine studies (five comparisons shown because one study included two fluoxetine arms that compared different doses of the drug) favored fluoxetine (SMD, -0.28; 95% CI, -0.42 to -0.14; I squared=0.0%; moderate SOE). For paroxetine, two studies (one that compared two doses of paroxetine with placebo) each found significant decreases in PTSD symptoms among paroxetine versus placebo subjects (CAPS SMD of -0.56, -0.46, or -0.44 in each study; moderate SOE). Although only three of the seven sertraline studies indicated significant benefit of sertraline for PTSD symptoms, the meta-analysis of pooled data indicated a significant but modest difference of about 5 points on the CAPS between groups (SMD, -0.20; 95% CI, -0.20; 95% CI, -0.36 to -0.04; low SOE). Studies that used other PTSD symptom assessments had consistent findings.[61, 71, 170, 174]

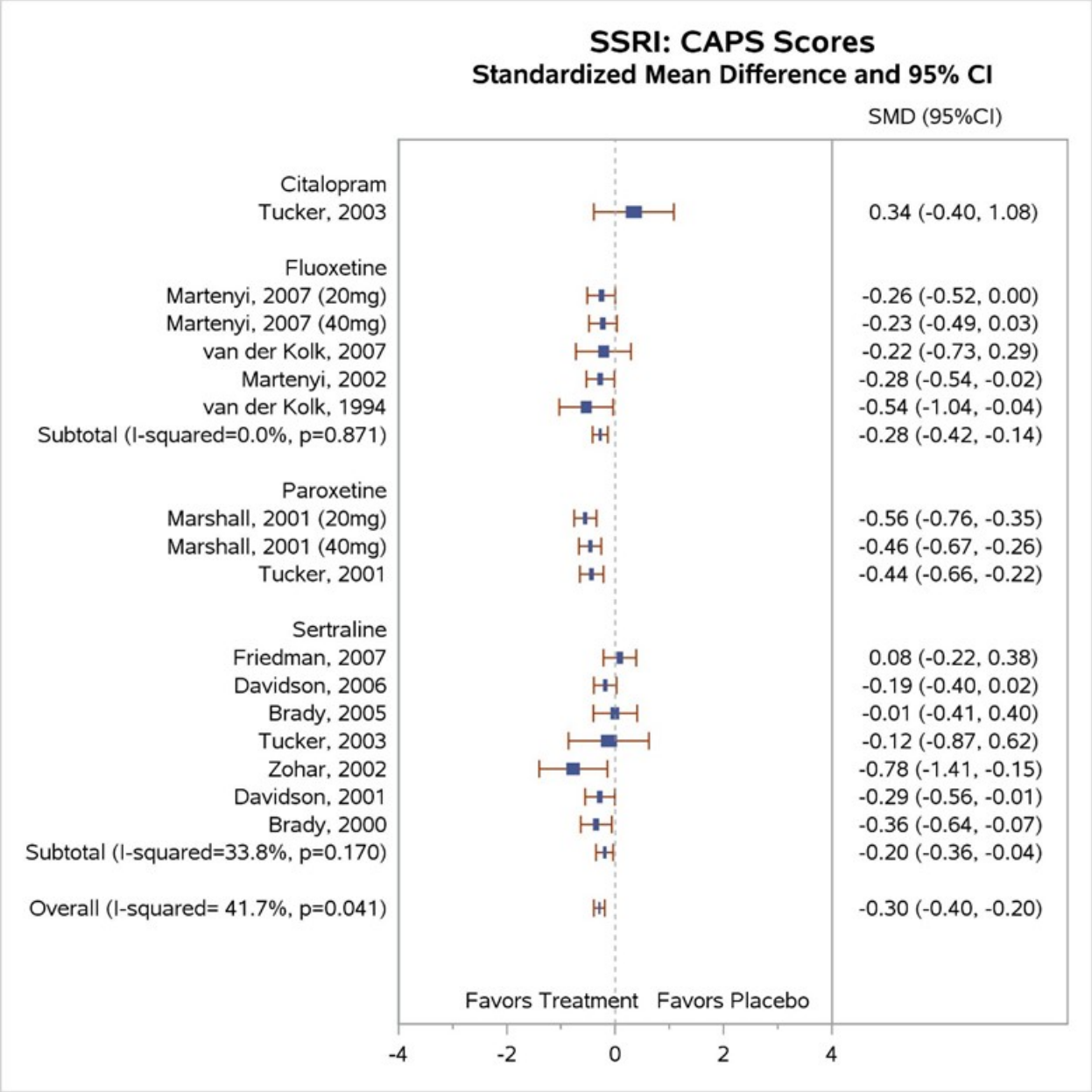
Remission

Two studies each favored paroxetine, one significantly so (RD, 0.13; p=0.008 in one large study[65] and RD, 0.19; p=0.34 in one small study;[174] moderate SOE). The other studies were single trials of fluoxetine[47] and sertraline[69] that each found slight (but insignificant) between-group differences in remission (insufficient SOE).

Loss of PTSD Diagnosis

A single fluoxetine study favored fluoxetine over placebo for loss of PTSD diagnosis (RD, 0.14, p=0.23) but not significantly so (insufficient SOE).[47]

Figure 22. Standardized mean change from baseline in CAPS for selective serotonin reuptake inhibitors compared with placebo



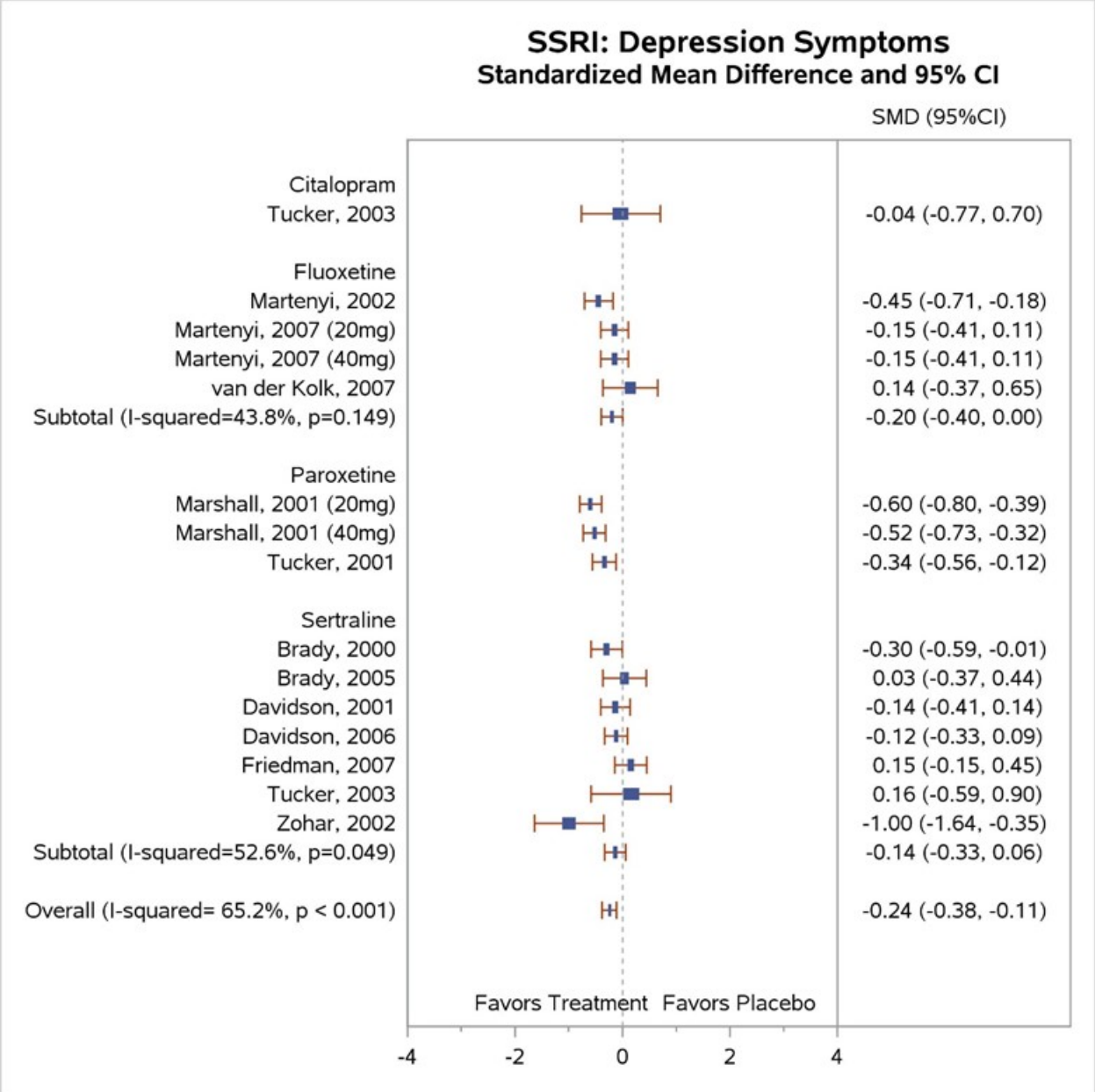
CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; PTSD = posttraumatic stress disorder; SMD = standardized mean difference; SSRI = selective serotonin reuptake inhibitor.

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Eleven of the SSRI studies reported between-group changes in depression symptoms (Figure 23). One small study provided insufficient evidence to determine efficacy of citalopram for reducing comorbid depression in adults with PTSD.[175] The three fluoxetine studies had mixed results with limited evidence of no between-group differences (low SOE for no difference); one study evidenced significant benefit of fluoxetine,[61] another study that tested two different doses of fluoxetine favored both drug arms but not significantly so,[62] and the third study found the placebo group to have nonsignificantly greater decreases in depression than fluoxetine

participants (p=ns).[47] Both paroxetine studies found significantly greater decreases among intervention group versus placebo group subjects in depression symptoms (moderate SOE).[64, 65] Decreases in depression symptoms at end-of-treatment did not differ between sertraline and placebo groups (SMD, -0.14; 95% CI, -0.33 to 0.06, 7 studies, N=1,085; low for no difference).

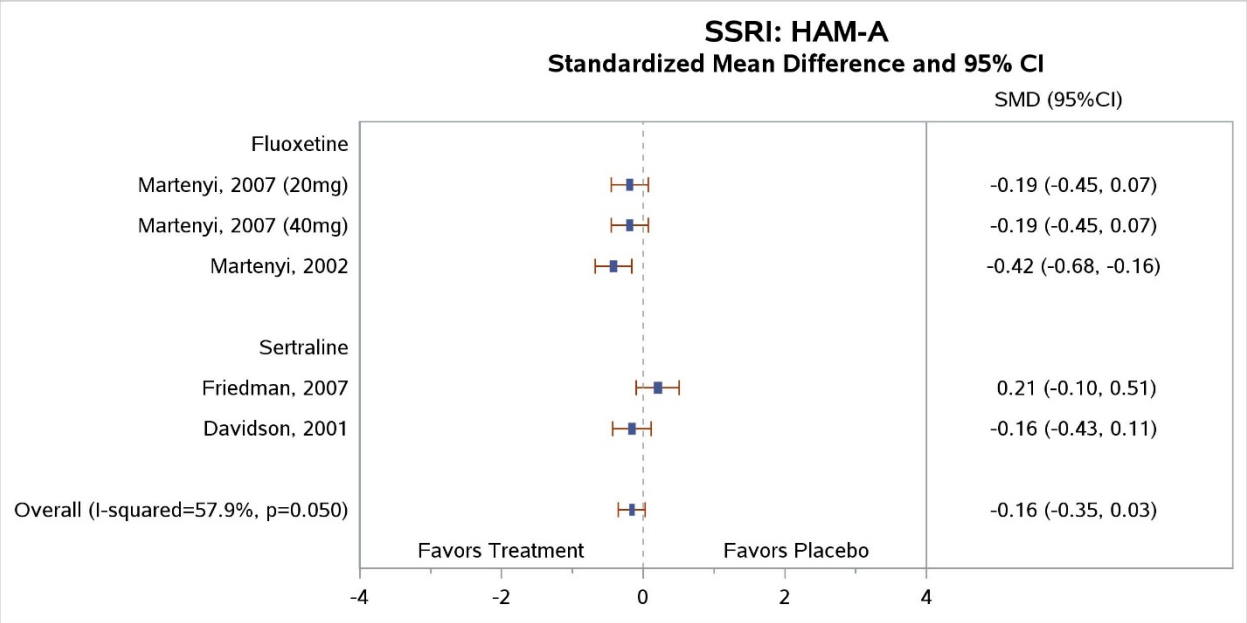
Figure 23. Standardized mean change from baseline in depressive symptoms for selective serotonin reuptake inhibitors compared with placebo



CI = confidence interval; SMD = standardized mean difference; SSRI = selective serotonin reuptake inhibitor.

Four studies assessed the efficacy of SSRIs for anxiety symptoms (Figure 24). Both fluoxetine studies favored the treatment group, but only one significantly so.[61, 62] The two sertraline studies found effect sizes in the opposite direction, with one study favoring sertraline and the other favoring placebo (insufficient SOE).[68, 70]

Figure 24. Standardized mean change from baseline in anxiety symptoms (HAM-A) for selective serotonin reuptake inhibitors compared with placebo



CI = confidence interval; HAM-A = Hamilton Anxiety Rating Scale; SMD = standardized mean difference; SSRI = selective serotonin reuptake inhibitor.

Quality of Life

Two studies of sertraline[66, 69] each demonstrated efficacy for quality of life, but only one significantly so (between-group mean difference, 2.4; p=ns in one study and between-group mean difference, 8.4; p<0.05 in another; low SOE).[66, 69]

Disability or Functional Impairment

Four studies assessed disability differences across SSRI and placebo groups. One study each of fluoxetine[170] and sertraline[69] provided limited evidence of group differences in disability assessment (insufficient SOE). Two studies[64, 65] provided evidence for the efficacy of paroxetine on pre- to posttreatment changes in disability (moderate SOE).

Detailed Synthesis: Serotonin and Norepinephrine Reuptake Inhibitors

Characteristics of Studies

Table 22 summarizes the characteristics of the two studies meeting our inclusion criteria. Further details describing the included studies are provided in Appendix F. Both studies evaluated venlafaxine extended release among a heterogeneous group of subjects with a variety of index trauma types. Both studies used CAPS to assess the primary outcome.

Table 22. Characteristics of included placebo-controlled trials of serotonin and norepinephrine reuptake inhibitors

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Davidson et al., 2006[73]	Venlafaxine ER 37.5 to 300 mg (161) Placebo (168)	24	Male and female Mixed	81 to 82.9	41	54	NR	Medium
Davidson et al., 2006[69]	Total 538[b] Venlafaxine 37.5 to 375 mg (179) Placebo (179)	12	Male and female Mixed	~82	NR	NR	NR	Medium

[a]Data reported are mean CAPS or range of mean CAPS scores across groups unless another instrument is specified.
[b]The Ns for each are the number analyzed and include a third study arm (sertraline 25 to 200 mg); the number randomized to each group was not reported (overall N was 538; 531 were included in the analysis).

CAPS = Clinician-Administered PTSD Scale; ER = extended release; F = female; mg = milligram; N = total number randomized/assigned to intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; y = year.

Results of Serotonin and Norepinephrine Reuptake Inhibitors

PTSD Symptoms

Both studies reported similar significant between-group decreases in CAPS-assessed PTSD symptoms from pre- to posttreatment (SMD of -0.35 and -0.26 across two individual studies; Appendix H; moderate SOE).[69, 73]

Remission

Both venlafaxine studies reported significant between-group differences in remission at the end of treatment assessment (RD of 0.12 and 0.15 in the 2 studies; moderate SOE). One also reported continued benefit at the 3-month followup assessment (RD, 0.13; moderate SOE).[73]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Both studies found significant benefit of venlafaxine for depression symptoms (HAM-D between-group mean difference of -2.6 and -1.6 in the 2 studies; moderate SOE).[69, 73]

Quality of Life

Both studies found significant benefit of venlafaxine for quality of life (Quality of Life Enjoyment and Life Satisfaction Short Form between-group mean difference of 2.8 and 4.1 in the 2 studies; moderate SOE).[69, 73]

Disability or Functional Impairment

Both studies found significant benefit of venlafaxine for disability (SDS between-group difference of -2.1 and -2.0 in the 2 studies; moderate SOE) and functioning (Global Assessment of Functioning between-group difference of 2.8 and 4.0 in the 2 studies; moderate SOE).[69, 73]

Detailed Synthesis: Placebo-Controlled Trials of Tricyclic Antidepressants

We did not find any trials comparing tricyclic antidepressants with placebo or other medications that had low or medium risk of bias.[179-182]

Detailed Synthesis: Placebo-Controlled Trials of Other Second-Generation Antidepressants

Table 23 summarizes the characteristics of the two studies that met our inclusion criteria. Further details describing the included studies are provided in Appendix F.

Table 23. Characteristics of included placebo-controlled trials of other second-generation antidepressants

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Becker et al., 2007[183]	Total 30[a] Bupropion 100 to 300 mg (18) Placebo (10)	8	Male and female Mixed	NR	50	21	71	Medium
Davidson et al., 2003[184]	Total 29[b] Mirtazapine 15 to 45 mg (17) Placebo (9)	8	Male and female Mixed	SPRINT 21.7 to 25.0	46	NR	NR	Medium

[a] Thirty subjects were randomized; exact numbers randomized to each group NR; authors reported that 18 received bupropion and 10 received placebo; 2 dropped out prior to treatment.

[b] A total of 29 subjects were randomized: 3 subjects dropped out early, 17 received mirtazapine, and 9 received placebo.

Note: When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

F = female; mg = milligram; N = total number randomized/assigned to intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; SPRINT = Short PTSD Rating Interview; y = year.

Of the two included small, placebo-controlled trials, one assessed bupropion[183] and one assessed mirtazapine.[184] Both studies enrolled a heterogeneous group of middle-aged subjects with a variety of index trauma types (e.g., military combat or war trauma, childhood sexual abuse, physical abuse, rape, MVA, witnessing a trauma, death or suicide of a loved one).

Results of Other Second-Generation Antidepressants

PTSD Symptoms

Both included studies reported various measures of PTSD symptoms.[183, 184] All analyses favored the treatment group, but most comparisons did not indicate significant differences across groups. Overall, we found insufficient evidence to determine the efficacy of either bupropion or mirtazapine for PTSD symptoms (insufficient SOE).

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

The single bupropion and single mirtazapine studies each favored the treatment group for depression symptoms, but differences did not reach statistical significance across groups (insufficient SOE).[183, 184] The mirtazapine study reported greater decreases in anxiety symptoms among the treatment versus placebo groups (between-group difference, -1.6, $p<0.05$; insufficient SOE); the bupropion study did not examine anxiety symptom outcomes.[184]

Detailed Synthesis: Head-to-Head (Comparative Effectiveness) Pharmacotherapy Trials

Characteristics of Studies

Table 24 summarizes the four studies that met inclusion criteria. Further details are provided in Appendix F. One study enrolled veterans randomized to paroxetine plus naltrexone (arm not eligible), paroxetine plus placebo, desipramine plus naltrexone (arm not eligible), or desipramine plus placebo.[185]

Table 24. Characteristics of included head-to-head pharmacotherapy trials

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
Davidson et al., 2006[69]	Total 538[b] Venlafaxine 37.5 to 375 mg (179) Sertraline 25 to 200 mg (173) Placebo (179)	12	Male and female Mixed	~82	NR	NR	NR	Medium
Petrakis et al., 2012[185]	Paroxetine 40 mg + Naltrexone 50 mg (22) (arm not eligible) Paroxetine 40 mg + Placebo (20) Desipramine 200 mg + Naltrexone 5 Placebo 0 mg (22) (arm not eligible) Desipramine 200 mg + (24)	12	Male and female Veterans w/alcohol dependence	62.5 to 77.8	47	9	25	Medium
Sonne et al., 2016[186]	Sertraline 25 to 200 mg (109) Venlafaxine 37.5 to 375 mg (98)	24-28	Trauma, affected refugees, Catastrophic experience Unknown what portion of the sample had clinical PTSD	HTQ 3.18 to 3.24	44	40	NR	Medium
Tucker et al., 2003[175] Tucker et al., 2004[176]	Citalopram 20 to 50 mg (25) Sertraline 50 to 200 mg (23) Placebo (10)	10	Male and female Mixed	83.9 to 94.2	39	74	14	Medium

[a]Data reported are mean CAPS or range of mean CAPS scores across groups unless otherwise specified.
[b]The Ns for each are the number analyzed; the number randomized to each group was not reported (overall N was 538; 531 were included in the analysis).

CAPS = Clinician-Administered PTSD Scale; F = female; mg = milligram; HTQ = Harvard Trauma Questionnaire; N = total number randomized/assigned to intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; y = years.

Results of Head-to-Head Pharmacotherapy Trials

PTSD Symptoms

All four studies assessed PTSD symptoms.[69, 175, 185, 186] The study that compared paroxetine+placebo versus desipramine+placebo found similar decreases in PTSD symptoms

across groups (CAPS between-group difference of -3.2 favoring desipramine+placebo, p=ns, insufficient SOE).[185] The studies that tested venlafaxine extended release (ER) versus sertraline also found similar decreases in PTSD symptoms across groups (CAPS between-group difference of -2.1 favoring sertraline, p=ns and Harvard Trauma Questionnaire between-group difference of -0.09 favoring sertraline, p=ns, low SOE for no difference).[69, 186] The fourth head-to-head trial favored sertraline over citalopram for PTSD symptom outcome comparisons; however, differences did not reach statistical significance (CAPS between-group difference of -11.1; p=ns; insufficient SOE).[175]

Remission

The one head-to-head trial that reported remission favored venlafaxine over sertraline for PTSD symptoms, but differences did not reach statistical significance (CAPS between-group mean difference of -5.9; p=ns, insufficient SOE).[69]

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

All four studies assessed depression symptoms.[69, 175, 185, 186] The study that compared paroxetine+placebo versus desipramine+placebo found similar decreases in depression symptoms across groups (HAM-D between-group difference of -1.3 favoring paroxetine+placebo, p=ns, insufficient SOE).[185] The studies that tested venlafaxine ER versus sertraline also found similar decreases in depression symptoms across groups (HAM-D between-group mean difference of -0.1 favoring venlafaxine, p=ns in one study and -0.7 in the other; moderate SOE for no difference). The fourth head-to-head trial favored citalopram over sertraline for depression symptoms; however, differences did not reach statistical significance (BDI between-group difference of -2.9; p=ns; insufficient SOE).[175]

One study that compared anxiety symptoms across groups found no differences between citalopram and sertraline groups (insufficient SOE).[186]

The study that tested paroxetine+placebo versus desipramine+placebo among veterans with comorbid alcohol dependence found greater decreases in the percentage of heavy drinking days (p=0.009) and drinks per drinking days (p=0.027) among subjects in the desipramine+placebo group than among those in the paroxetine+placebo group (low SOE).[185]

Quality of Life

Two studies compared the efficacy of venlafaxine ER and sertraline for quality-of-life outcomes. One study favored venlafaxine[69] and the other favored sertraline,[186] but the differences across treatments did not reach statistical significance in either study (low SOE for no difference).

Disability or Functional Impairment

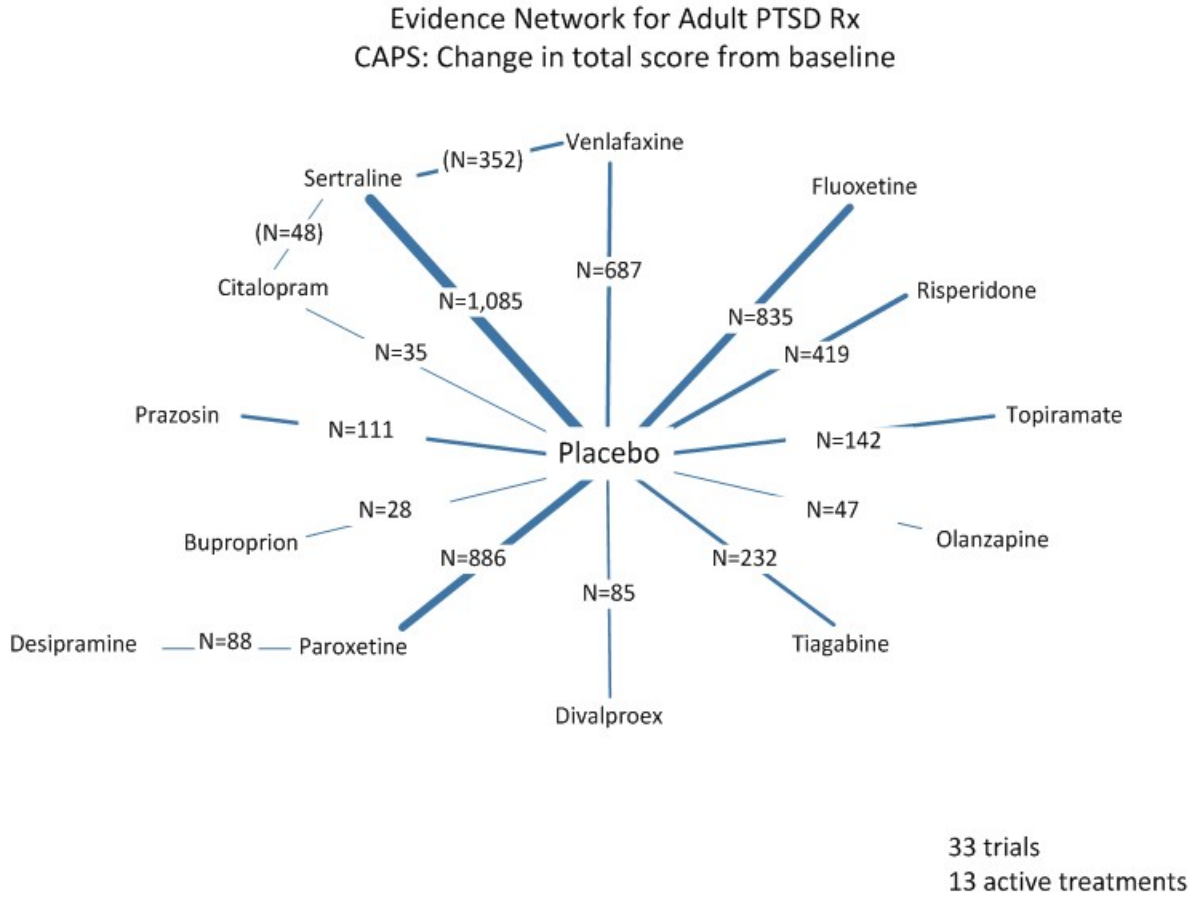
The findings for disability differences across groups mirrored those for quality-of-life differences. That is, two studies compared the efficacy of venlafaxine ER and sertraline for disability outcomes. One study favored venlafaxine[69] and the other favored sertraline,[186] but the differences across treatments did not reach statistical significance in either study (low SOE for no difference).

Network Meta-Analysis of Pharmacotherapy Trials

We conducted network meta-analyses on pre- to posttreatment decreases in PTSD symptoms as measured by the CAPS to determine the comparative effectiveness of drug treatments using all efficacy and comparative effectiveness evidence compiled to answer KQ 2. We did this after checking for any obvious transitivity which would preclude the use of network meta-analysis due to inconsistencies in the sample or treatment characteristics. We did not find any such inconsistencies.

Our network meta-analysis included 33 trials and 13 active treatments (4,491 subjects) that included CAPS-measured PTSD symptoms. A network diagram illustrates the number of subjects contributing to each comparison; thickness of lines connecting each drug-drug or drug-placebo comparison indicates the number of trials with available data for that comparison (Figure 25).

Figure 25. Evidence network: comparisons, and number of subjects for each, included in network meta-analysis[a]



[a]Sample sizes may not add up to those in the diagram because of multiarm studies.
CAPS = Clinician-Administered PTSD Scale; N = number; PTSD = posttraumatic stress disorder.

We conducted two tests to assess the consistency for the network meta-analysis. First, we compared consistency and inconsistency models that did not differ significantly ($\chi^2(3)=0.06$, p=0.997). Next, when possible given the network structure, we tested for differences between

direct and indirect estimates using network sidesplits. Direct and indirect estimates did not differ significantly for any of the sidesplit comparisons (Table 25).

Table 25. Consistency of network meta-analysis finding

		Direct			Indirect			Difference		
Drug A	**Drug B**	**Coefficient**	**95% CI**	**p**	**Coefficient**	**95% CI**	**p**	**Coefficient**	**95% CI**	**p**
Citalopram	Sertraline	-0.45	-1.02, 0.12	0.122	-0.60	-1.98, 0.79	0.398	0.15	-1.36, 1.65	0.849
Despiramine	Paroxetine	0.14	-0.28, 0.56	0.507	-0.41	-124.40, 123.59	0.995	0.55	-123.45, 124.54	0.993
Sertraline	Venlafaxine	-0.07	-0.32, 0.17	0.556	-0.08	-0.37, 0.20	0.566	0.01	-0.36, 0.39	0.955

Figure 26 presents the network meta-analysis findings for each between-group treatment comparison of pre- to posttreatment change in CAPS-assessed PTSD symptoms (SMD and 95% CI displayed for each comparison). We report the findings on the pharmacological interventions for which analyses in the prior section of this report determined at least moderate SOE of efficacy for PTSD symptoms (fluoxetine, paroxetine, and venlafaxine).

Our network meta-analysis evidenced no significant differences between effectiveness of paroxetine, fluoxetine, and venlafaxine.

Indirect evidence from placebo-controlled trials contributed the majority of evidence to the network meta-analysis. Only four head-to-head comparisons contributed data to the network, none of which compared effectiveness between interventions determined to have at least moderate SOE of efficacy for PTSD symptoms (fluoxetine, paroxetine, and venlafaxine); because indirect comparisons provided the basis for most of the network meta-analysis, we believe the findings only support a low SOE of benefit.

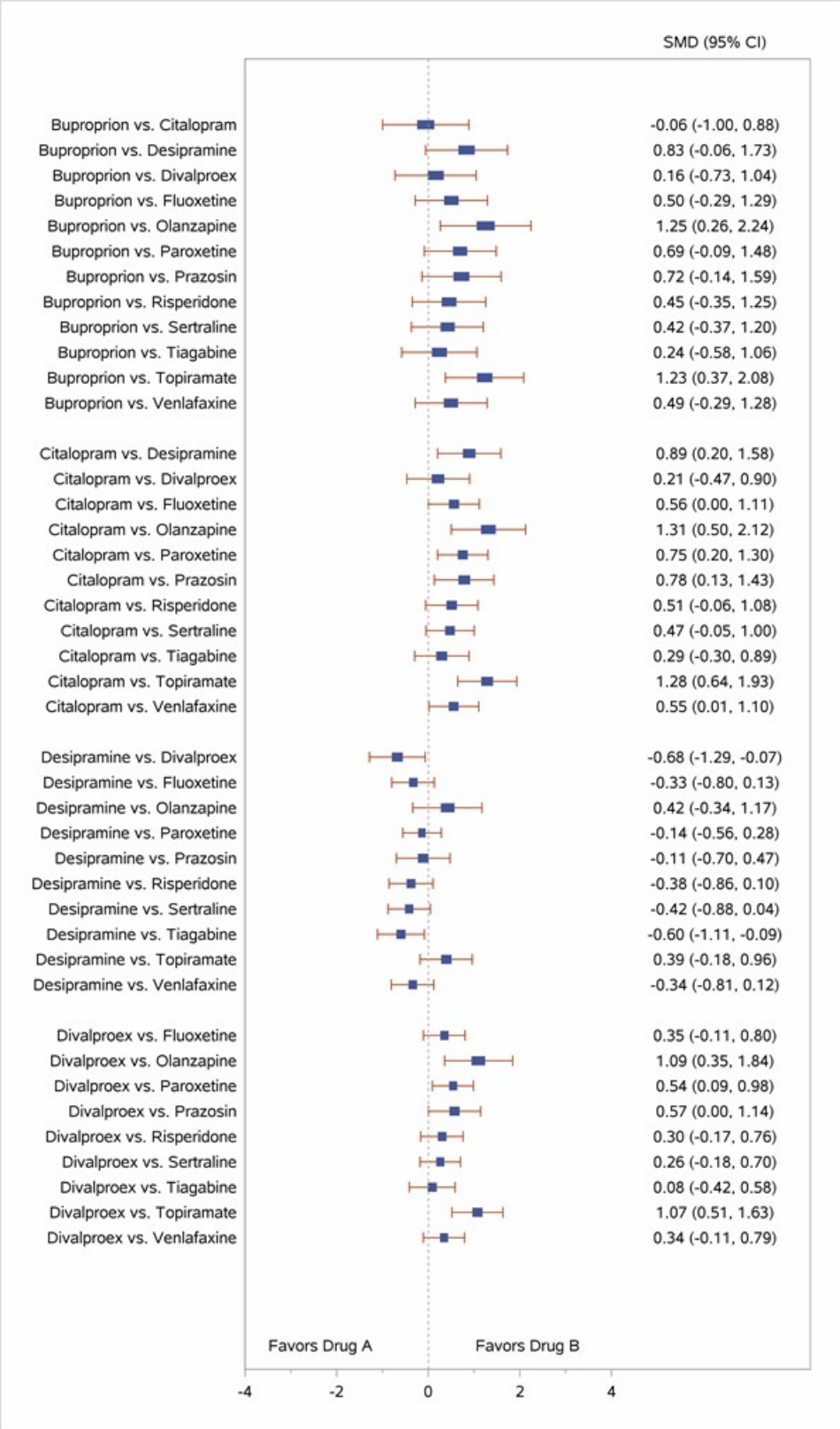
KQ 2a. Variability in Efficacy or Comparative Effectiveness of Pharmacological Interventions by Patient Characteristics or Type of Trauma

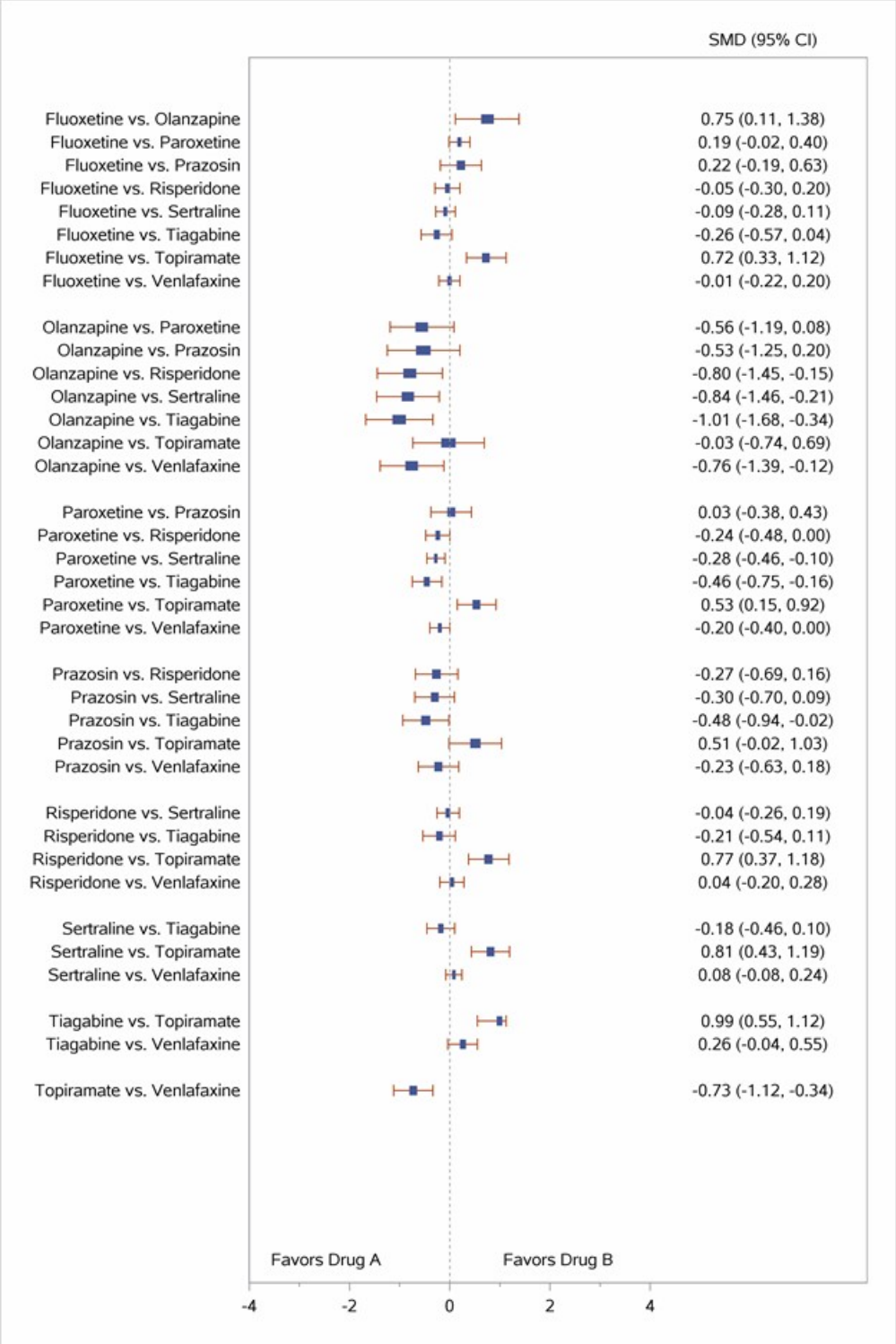
This KQ evaluated whether the efficacy or comparative effectiveness of any of the pharmacological interventions differed by patient characteristics or type of trauma experienced. To answer this question, we present findings from included studies that reported outcomes for subgroups of interest (defined by patient or trauma factors) and compare the efficacy or comparative effectiveness across subgroups. One study provided information about the efficacy of a pharmacological intervention across different subgroups of interest.

Key Point

- One study compared the efficacy of fluoxetine versus placebo between subjects with child- versus adult-onset trauma and found no differences in efficacy by trauma onset (insufficient SOE for a single study of unknown consistency and imprecise findings).

Figure 26. Results of network meta-analysis comparing improvement in PTSD symptoms (change in CAPS total score)





CAPS = Clinician-Administered PTSD Scale; N = number; CI = confidence interval; PTSD = posttraumatic stress disorder; SMD = standardized mean difference.

Detailed Synthesis: Patient Characteristics or Trauma Types

Characteristics of Included Studies

Table 26 summarizes the characteristics of the included study previously described in this report. The study had an end of treatment assessment at 8 weeks and a 6-month followup that included the CAPS as the primary outcome measure of PTSD symptoms. Additional details describing the included study can be found in Appendix F.

Table 26. Characteristics of included pharmacological trials that compared efficacy or comparative effectiveness between subgroups defined by patient characteristics or trauma types

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
van der Kolk et al., 2007[47]	EMDR (29) Fluoxetine (30) Placebo (29)	8 weeks (6 months)	Male and female Mixed subgroup analysis: child-onset and adult-onset trauma	71.2	36	83	33	Medium

[a] Data reported are mean CAPS total or range of mean CAPS total scores across groups unless otherwise specified.

CAPS = Clinician-Administered PTSD Scale; EMDR = eye movement desensitization and reprocessing; N = total number randomized/assigned to intervention and control groups; PTSD = posttraumatic stress disorder; y = year.

The analysis conducted to answer this KQ had a small sample size, and therefore did not have the statistical power to detect anything but a very large difference. Many factors other than patient characteristics and trauma type varied across studies, which prevented us from conducting further subgroup analyses using studies that did not, a priori, seek to examine differences in efficacy or comparative effectiveness of interventions across subgroups. Thus, findings should be considered hypothesis generating.

The single study compared EMDR, fluoxetine, and placebo in subjects with a variety of trauma types including child sexual abuse, child physical abuse, child sexual and physical abuse, adult sexual assault, adult physical assault, domestic violence, other adult victimization, traumatic loss, war/terror/violence, and injury/accident.[47] The authors reported subgroup analyses for those with child-onset trauma and those with adult-onset trauma.

Efficacy or Comparative Effectiveness by Patient Characteristic or Trauma Type

The study compared the efficacy of fluoxetine versus placebo between those with childhood-onset (prior to age 18) versus adult-onset trauma.[47] No significant index trauma onset by treatment differences was found in the efficacy of fluoxetine compared with placebo by trauma onset (child versus adult) as tested by interaction analysis.

KQ 3. Psychotherapy Versus Pharmacotherapy for Adults With PTSD

This KQ focused on studies that directly compared a psychological treatment with a pharmacological treatment.

Key Point

- One study that tested the comparative effectiveness of EMDR versus fluoxetine for reduction in PTSD symptoms, rates of symptom remission, and loss of PTSD diagnosis and found insufficient evidence to draw conclusions.

Detailed Synthesis

Characteristics of Studies

We found one medium risk of bias study that met our inclusion criteria. Table 27 summarizes the characteristics of the study. Further details are provided in Appendix F.

One study compared subjects with varying trauma types randomized to 8 weeks of fluoxetine, EMDR, or placebo.[47] Prior KQ 1 and KQ 2 results sections include findings from the placebo comparisons.

Table 27. Characteristics of included studies directly comparing psychotherapy with pharmacotherapy

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
van der Kolk, 2007[47]	Fluoxetine (30)[b] EMDR (29) Placebo (29)	8 weeks (6 months)	Male and female Mixed	71	36	83	33	Medium

[a]Data reported are mean CAPS total score (1 week). The mean CAPS total score (1 month) was 74.0.
[b]Titrated from 10 mg/day to max 60 mg/day (mean = 30 mg/day, mode = 40 mg/day).

CAPS = Clinician-Administered Post Traumatic Stress Disorder Scale; EMDR = eye movement desensitization and reprocessing; N = total number randomized/assigned to intervention and control groups; PTSD = posttraumatic stress disorder; y = year.

Results for Psychotherapy Versus Pharmacotherapy

PTSD Symptoms

EMDR and fluoxetine groups did not have significant differences in pre- to posttreatment decreases in CAPS-assessed PTSD symptoms (between-group mean difference, -10.1 favoring fluoxetine; p=0.13; insufficient SOE). EMDR group subjects, however, had significantly greater decreases in PTSD symptoms than fluoxetine group subjects measured at the 6-month followup assessment (between-group mean difference, -16.3; p<0.005; insufficient SOE).

Remission

Comparisons favored EMDR-treated subjects compared with fluoxetine-treated subjects for remission at both the end of treatment and 6-month followup assessments, but only the followup comparisons reached statistical significance (end of treatment RD, 0.15; p=0.17; 6-month followup RD, 0.58, p<0.001; insufficient SOE).

Loss of PTSD Diagnosis

The percentages of subjects no longer meeting diagnostic criteria for PTSD were similar for EMDR compared with fluoxetine at the end of treatment (RD, 0.03 favoring EMDR; p=0.82; insufficient SOE) and 6-month followup assessment (RD, 0.15, p=0.20; insufficient SOE).

Prevention or Reduction of Comorbid Medical or Psychiatric Conditions

Comparisons favored EMDR-treated subjects compared with fluoxetine-treated subject for depression symptoms at both the end of treatment and 6-month followup assessments, but only the followup comparisons reached statistical significance (BDI end of treatment between-group mean difference, -1.9; p=ns; 6-month followup between-group mean difference, -6.8, p<0.001; insufficient SOE).

KQ 3a. Variability in Comparative Effectiveness of Psychological Versus Pharmacological Interventions by Patient Characteristics or Type of Trauma

This KQ evaluated whether the efficacy or comparative effectiveness of psychological and pharmacological interventions differed by patient characteristics or types of trauma experienced. To answer this question, we present findings from included studies that reported outcomes for subgroups of interest (defined by patient or trauma factors) and compare the efficacy or comparative effectiveness across subgroups. One study provided information about the comparative effectiveness of a psychological and a pharmacological intervention across different subgroups of interest.

Key Point

- One study evaluated the comparative effectiveness of EMDR versus fluoxetine between those with child- and adult-onset trauma (insufficient SOE).

Detailed Synthesis: Patient Characteristics or Trauma Types

Characteristics of Included Studies

Table 28 summarizes the characteristics of the one included study previously described in this report. The study had an end of treatment assessment at 8 weeks and a 6-month followup that included the CAPS as the primary outcome measure of PTSD symptoms. Additional details describing the included study can be found in Appendix F.

Table 28. Characteristics of included psychological versus pharmacological trials that examined comparative effectiveness between subgroups defined by patient characteristics or trauma types

Study	Arm (N)	Duration (Followup)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female	% Non-white	Risk of Bias
van der Kolk et al., 2007[47]	EMDR (29) Fluoxetine (30) Placebo (29)	8 weeks (6 months)	Male and female Mixed subgroup analysis: child-onset and adult-onset trauma	71.2	36	83	33	Medium

[a] Data reported are mean CAPS total or range of mean CAPS total scores across groups unless otherwise specified.

CAPS = Clinician-Administered PTSD Scale; EMDR = eye movement desensitization and reprocessing; N = total number randomized/assigned to intervention and control groups; PTSD = posttraumatic stress disorder; y = year.

One study compared EMDR, fluoxetine, and placebo in subjects with a variety of trauma types.[47] The authors reported comparisons between the comparative effectiveness of EMDR versus fluoxetine between those with child- and adult-onset trauma.

Comparative Effectiveness by Patient Characteristics or Trauma Type

The study examined the comparative effectiveness of EMDR versus fluoxetine between those with childhood-onset (prior to age 18) versus adult-onset trauma.[47] Analyses indicated no significant differences in the comparative effectiveness of EMDR and fluoxetine between those with child- and adult-onset trauma (insufficient SOE).

KQ 4. Adverse Effects of Treatments for PTSD

For this question, we evaluated the studies included in KQs 1 through 3. In addition, we searched for non-RCTs and observational studies (specifically, prospective cohort studies with an eligible comparison group, and case-control studies). We did not find any nonrandomized trials or observational studies that met our inclusion criteria (e.g., prospective cohort studies or case-control studies with a sample size of at least 500; see the Methods section), nor did we exclude any observational studies solely for having a smaller sample size. Therefore, the results for this KQ included AE data from studies included in KQs 1 through 3. Throughout this section, we describe risks of various AEs reported as absolute RDs between intervention and control. Appendix F includes detailed information about specific AE findings for each study. Appendix G contains detailed information about the inputs to determine the SOEs of each study.

Key Points: Adverse Effects of Psychological and Pharmacological Treatments for Adults With PTSD

- Studies typically did not report the use of methods to systematically capture AE information collected by standardized measures.
- The few head-to-head trials provided insufficient evidence to compare AEs across different interventions.
- Insufficient SOE provides information regarding AEs associated with psychological treatments.
- Insufficient SOE provides information regarding most specific AEs such as mortality, suicidality, self-harmful behaviors, and withdrawals due to AEs for pharmacological treatments.
- Placebo comparisons of specific AEs between pharmacological treatments with at least moderate SOE of efficacy indicated small increased risk of the following AEs:
  - nausea, somnolence, and diarrhea for fluoxetine versus placebo (low SOE)
  - nausea, dry mouth, and somnolence for paroxetine versus placebo (low SOE)
  - nausea (moderate SOE), dry mouth (low SOE) and constipation (low SOE) for venlafaxine versus placebo

Detailed Synthesis: Psychological Treatments

Characteristics of Studies

The KQ 1 section of the report described brief characteristics of psychological studies rated low or medium risk of bias that included AE assessments. Appendix F contains full information about AE reporting and outcomes for each study.

Withdrawals Due to Adverse Effects

Just 3 of the 31 CBT-M studies,[31, 32, 36] 1 of the 25 CBT-exposure studies;[18] and 2 of the 10 EMDR studies[43, 48] reported information about withdrawals due to AEs (insufficient SOE).

Mortality

Just four CBT-exposure studies reported mortality.[12, 20, 138, 139] The CBT-exposure groups totaled two deaths across studies; six deaths occurred in the comparator groups (PCT, wait-list, or treatment as usual; insufficient SOE).

Suicide, Suicidal Ideation, or Self-Harmful Behaviors

Eleven of the included studies from KQ 1 reported information about suicide or self-harm—1 of 12 CBT-cognitive intervention studies,[127] 1 of 10 CBT-coping skills studies,[136] 5 CBT-exposure studies,[12, 20, 53, 138, 139] and 2 of 31 CBT-M studies.[23, 144] Studies that did report suicidality reported few occurrences of several different suicidality measures and self-harm behaviors (insufficient SOE).[12]

Other Specific Adverse Effects

A few studies included other measures of AEs such as symptom deterioration, hospitalizations, and serious AEs (Appendix F), but most tested different interventions, comparators, and outcomes that limit the ability to synthesize the data to make definitive conclusions.

Detailed Synthesis: Pharmacological Treatments

Characteristics of Studies

The KQ 2 section of the report described brief characteristics of pharmacological studies rated low or medium risk of bias that provided the evidence base for the assessment of AEs of pharmacological interventions.

Withdrawals Due to Adverse Effects

All but six[47, 63, 76, 82, 165, 175] of the pharmacotherapy studies reported data on withdrawals due to AEs (data shown in Appendix F). The wide variation in interventions and comparators, however, precluded the ability to pool evidence to determine differences across most pharmacotherapy groups (insufficient SOE). Appendix H displays the meta-analysis pooled findings of anticonvulsants, antipsychotics, and SSRIs. The analysis of pooled data likely does not have adequate power to detect significant differences, although RDs of individual and pooled studies do not appear to indicate a clinically meaningful difference in withdrawals due to AEs across treatment groups (insufficient SOE). Appendix G provides additional details for SOE grades.

Mortality

Only three of the pharmacotherapy studies reported mortality.[62, 69, 165] Across these studies, one death occurred in the pharmacotherapy group (which authors did not deem related to use of the drug) and one in the comparator group (insufficient SOE).[62, 69, 165] Appendix F contains additional details about the specific number of AEs reported in each study.

Suicide, Suicidal Ideation, or Self-Harmful Behaviors

Four of the included medication studies reported data on suicidality using various measures or self-harmful behaviors.[62, 76, 165, 174] Few reported events in each study, and the inability to determine the relationship with the drug itself precludes conclusions about these associations (insufficient SOE). Appendix F contains additional details about the specific number of AEs reported in each study.

Other Specific Adverse Effects, by Medication

Limited information about specific AEs reported for most of the medications precluded synthesis of these findings. We therefore focus here on the medications with moderate SOE supporting efficacy (see KQ 2)—fluoxetine, paroxetine, and venlafaxine—to conduct additional meta-analyses for specific AEs. Appendix F contains additional details about the specific number of AEs reported in each study.

SSRIs Compared With Placebo

Fluoxetine Compared With Placebo

Of the five studies that compared fluoxetine with placebo, three reported data on some specific AEs (additional details available in Appendix F).[62, 63, 173]

Overall, insufficient findings for fluoxetine prevented determination of between-group differences in specific AEs. Three studies (total N=756) contributed data about specific AEs, with most specific AEs only reported by one study each. Evidence from two studies[62, 173] suggests increases, although not statistically significant in either study, in the risk of nausea (RD range 0.03 to 0.07; p=ns; N=712; low SOE) and somnolence (RD range 0.04 to 0.06 [variation by dose of fluoxetine]; p=ns; 1 study; N=411). Another small fluoxetine study found large, statistically significant differences in the risk of diarrhea among fluoxetine versus placebo subjects (RD, 0.24, p<0.05; 1 study; N=44; low SOE).

Paroxetine Compared With Placebo

Of the three studies that compared paroxetine with placebo, two reported data for a few specific AEs.[65, 174] The third provided more ambiguous summary data of specific AEs.[64]

Overall, evidence from paroxetine studies was insufficient to determine whether the RD of most specific AEs between drug and placebo. Single studies reported events for just a few outcomes; few events occurred. Evidence from a single study (N=323) did suggest a significant increase in nausea (RD, 0.11; p<0.05), dry mouth (RD, 0,10; p<0.05), and somnolence (RD, 0.13; p<0.05). Studies provided limited data for other specific AEs (insufficient SOE).

Venlafaxine Compared With Placebo

Of the two studies that compared venlafaxine with placebo (total N=687), both reported data on several specific AEs.[69, 73] Overall, findings suggest statistically significant increases in the venlafaxine compared with placebo group subjects in the risk of nausea (RD, 0.10 in both individual studies, p<0.05 in both studies; moderate SOE), dry mouth (RD, 0.04; p=ns in one study; RD, 0.08; p<0.05 in the other study; low SOE), and constipation (RD, 0.02; p=ns in one study; RD, 0.09; p<0.05 in the other study, low SOE). No studies found significant differences in insomnia, fatigue, somnolence, or decreased appetite between venlafaxine- versus placebo-treated adults with PTSD (insufficient SOE).

Detailed Synthesis: Head-to-Head Studies of Psychological and Pharmacological Interventions

No KQ 3 studies reported AEs.

Contextual Question (CQ) 1a. Components of Effective Psychological Treatments

For this CQ, we searched for articles that examined the components of effective psychological treatments (e.g., frequency or intensity of therapy and/or aspects of the therapeutic modality). We found only one recently published article that addressed this CQ.[187] The article, authored by "pioneer" creators of an empirically based psychotherapy to treat PTSD, focuses on components of their treatment believed to be most critical in its effectiveness. The review article synthesizes the collected information to conclude that most frequently identified components include psychoeducation, coping skills and emotion regulation, cognitive processing and restructuring (i.e., "meaning making"), IE, emotions, and memory processing.

CQ 1b. Degree of Fidelity of Psychological Interventions Effective in Trial Settings When Implemented in Clinical Practice Settings

For this CQ, we searched for articles that aimed to determine the degree of fidelity of psychological interventions effective in trial settings when implemented in clinical practice settings. We found no direct evidence to help answer this CQ. We comment on the fidelity assessment of each psychological intervention in our risk of bias assessment included in Appendix E, but none of these studies or others we identified in our searches specifically tested the application of implementing efficacious interventions in clinical settings.

Discussion

We aimed to update a systematic review and meta-analysis of the comparative effectiveness and harms of psychological and pharmacological interventions for adults with posttraumatic stress disorder (PTSD). In the context of continued disagreement on treatment efficacy, we first assessed evidence for efficacy of the treatments of interest and then assessed comparative effectiveness. We also used this approach because few head-to-head comparative effectiveness trials exist, requiring us to rely on indirect evidence to make conclusions.

Below, we summarize the main findings and strength of evidence (SOE) by Key Question (KQ). We then discuss the findings in relation to what is already known, applicability of the findings, implications for decisionmaking, limitations, research gaps, and conclusions. When we have graded evidence as insufficient, it indicates that evidence is either unavailable, does not permit estimation of an effect, or does not permit us to draw a conclusion about efficacy or lack of efficacy (i.e., no differences between groups) with at least a low level of confidence.

Key Findings and Strength of Evidence

We synthesize the evidence base from studies rated as having low or medium risk of bias. We include commentary on the consistency of the findings from studies rated as having high risk of bias with our main findings in Appendix G. Like the prior review that conducted quantitative sensitivity analysis to understand differences between including and excluding studies with high risk of bias, we did not find inconsistency in the findings. In general, findings of studies with high risk of bias had similar magnitude of effects and confidence intervals (CIs) for observed outcomes as findings from studies with low and medium risk of bias.

The proportions of included studies and excluded studies for high risk of bias had similar sample characteristics and tested largely the same types of interventions and comparators (see Appendix G for tables). This suggests the body of evidence from low and moderate risk of bias studies included in this report is representative of the total set of studies that also includes high risk of bias study.

KQ 1. Psychological Treatments

Among the psychological treatments, studies of cognitive behavioral therapy (CBT)-exposure therapy and CBT-mixed (CBT-M) therapies provide high SOE supporting efficacy for PTSD symptoms and loss of PTSD diagnosis (high SOE). Moderate SOE supports the efficacy of cognitive processing therapy (CPT), cognitive therapy (CT), and eye movement desensitization and reprocessing (EMDR) for PTSD symptoms and loss of PTSD diagnosis (narrative exposure therapy [NET] also had moderate SOE for PTSD symptoms and low SOE for loss of diagnosis). Studies support low SOE for the efficacy of brief eclectic psychotherapy (BEP) for PTSD symptoms and loss of diagnosis and of imagery rehearsal therapy (IRT) and trauma affect regulation (TAR) for PTSD symptoms. Low SOE exists for no differences in efficacy of the Seeking Safety (SS) intervention for PTSD symptoms. Studies testing meta-cognitive therapy (MCT), stress inoculation therapy (SIT), relaxation, structured approach therapy (SAT), mindfulness-based stress reduction (MBSR), neurofeedback, emotional freedom therapy (EFT), memory specificity training (MEST), and interpersonal therapy (IPT) have insufficient evidence to support the efficacy for each of the PTSD outcomes of interest (PTSD symptoms, remission, loss of diagnosis).

Effect sizes for the psychological treatments graded as having moderate or high SOE supporting efficacy in decreasing PTSD symptoms were generally large (e.g., a minimum of a 22-point decrease in Clinician-Administered PTSD Scale (CAPS) and Cohen's d of less than -1.0). Table 29 summarizes the main findings and SOE for the psychological treatments with evidence of efficacy. The outcomes in the table include the three most frequently reported outcomes included in studies testing PTSD treatments: two of three PTSD outcomes of interest (PTSD symptom reduction and loss of PTSD diagnosis) and depression symptom reduction. Studies testing each psychological intervention of interest yielded insufficient SOE grades for the third PTSD outcome of interest, symptom remission, primarily because very few psychological studies reported remission as an outcome. Similarly, with the exception of depression symptoms, SOE for other outcomes of interest such as anxiety symptoms, substance use indicators, quality of life, disability or functional impairment, and return to work or active duty was generally graded as insufficient due to few studies reporting these outcomes. We noted a few exceptions: some evidence supported efficacy of CT for improving anxiety symptoms and disability and of CBT-M for anxiety and substance use (moderate SOE); and low SOE of efficacy for CBT-exposure treatments and BEP for improving anxiety symptoms and CBT-M for disability and functional impairment. Studies also indicated limited evidence of efficacy for SS intervention for PTSD symptoms (low SOE for no difference). Table 29 summarizes the available efficacy evidence and SOE for PTSD symptoms, loss of PTSD diagnosis, and depression symptoms.

Table 29. Summary of efficacy and strength of evidence of PTSD psychological treatments

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Cognitive processing therapy	PTSD symptoms[a]	5 (399)[1-4, 6]	Reduced PTSD symptoms SMD -1.35 (95% CI, -1.77 to -0.94)	Moderate
	Loss of PTSD diagnosis	4 (299)[1-4]	Greater loss of PTSD diagnosis RD 0.44 (95% CI, 0.26 to 0.62)	Moderate
	Depression symptoms[b]	5 (399)[1-6]	Reduced depression symptoms SMD -1.09 (95% CI, -1.52 to -0.65)	Moderate
Cognitive therapy	PTSD symptoms[a]	4 (283)[5, 7-9]	Reduced PTSD symptoms SMD of individual studies range from -2.0 to -0.3	Moderate
	Loss of PTSD diagnosis	4 (283)[5, 7-9]	Greater loss of PTSD diagnosis RD 0.55 (95% CI, 0.28 to 0.82)	Moderate
	Depression symptoms[b]	4 (283)[5, 7-9]	Reduced depression symptoms Between-group mean differences of individual trials range from -11.1 to -8.3	Moderate

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Cognitive behavioral therapy-exposure	PTSD symptoms[a]	12 (773)[3, 10-20]	Reduced PTSD symptoms SMD -1.23 (95% CI, -1.50 to -0.97)	High
		7 (577)[3, 10, 11, 13, 16, 18, 20]	SMD CAPS -1.12 (95% CI, -1.42 to -0.82)	
	Loss of PTSD diagnosis	5 (343)[3, 13, 14, 16, 17]	Greater loss of PTSD diagnosis RD 0.56 (95% CI, 0.35 to 0.78)	High[c]
	Depression symptoms[b]	9 (649)[3, 11-15, 18-20]	Reduced depression symptoms SMD -0.76 (95% CI, -0.91 to -0.60)	High
Cognitive behavioral therapy-mixed	PTSD symptoms[a]	21 (1,349)[12, 14, 22-40]	Reduced PTSD symptoms SMD -1.01 (95% CI, -1.28 to -0.74)	High[c]
		11 (709)[22, 23, 27-29, 34-39]	SMD -1.24 (95% CI, -1.67 to -0.81)	
	Loss of PTSD diagnosis	9 (474)[22-24, 31-34, 39, 41]	Greater loss of PTSD diagnosis RD 0.29 (95% CI, 0.17 to 0.40)	High[c]
	Depression symptoms[b]	10 (715)[3, 11-15, 18-21]	Reduced depression symptoms SMD -0.87 (-1.14 to -0.61)	High[c]
Eye movement desensitization and reprocessing	PTSD symptoms[a]	8 (449)[13, 16, 43-48]	Reduced PTSD symptoms SMD -1.08 (95% CI, -1.82 to -0.35)	Moderate[d]
	Loss of PTSD diagnosis	7 (427)[13, 16, 43-45, 47, 48]	Greater loss of PTSD diagnosis RD 0.43 (95% CI, 0.25 to 0.61)	Moderate
	Depression symptoms[b]	7 (347)[13, 43-48]	Reduced depression symptoms SMD -0.91 (95% CI, -1.58 to -0.24)	Moderate
Brief eclectic psychotherapy	Loss of PTSD diagnosis	3 (96)[49-51]	Greater loss of PTSD diagnosis RD of individual studies ranged from 0.13 to 0.58	Low
	Depression symptoms[b]	3 (96)[49-51]	Reduced depression symptoms Different depression scales used; all 3 studies favored treatment (3 of 3 studies p<0.05)	Low
Imagery rehearsal therapy	PTSD symptoms[a]	1 (168)[52]	Reduced PTSD symptoms Between-group mean difference--21.0; p<0.05	Low
Narrative exposure therapy	PTSD symptoms[a]	3 (232)[53-55]	Reduced PTSD symptoms SMD ranged from -1.95 to -0.79 across 3 individual studies	Moderate
	Loss of PTSD diagnosis	2 (198)[53, 54]	Greater loss of PTSD diagnosis RD of 0.06 and 0.43 in individual studies	Low

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Seeking Safety	PTSD symptoms[a]	3 (232)[56-58]	Reduced PTSD symptoms SMD of individual trials ranged from -0.22 to 0.04	Low for no difference
Trauma affect regulation	PTSD symptoms[a]	2 (173)[59, 60]	Reduced PTSD symptoms Between-group mean difference of -17.4 and -2.7 in individual studies	Low

NOTE: Outcomes graded as insufficient are not included in this table.

[a] SMD from the Clinician-Administered PTSD Scale and from other various PTSD symptom scales.
[b] SMD from the Beck Depression Inventory and from other various depression symptom scales.
[c] SOE increased from moderate to high because of additional evidence of efficacy published since prior PTSD review.
[d] SOE increased from low to moderate because of additional evidence of efficacy published since prior PTSD review.

CI = confidence interval; N = number of subjects; PTSD = posttraumatic stress disorder; RD = risk difference; SMD = standardized mean difference; SOE = strength of evidence.

Most of the direct head-to-head comparative evidence yielded insufficient evidence of differences in effectiveness across different types of psychotherapies. Of note, a few exceptions include evidence of greater effectiveness for CBT-exposure therapy than for relaxation for PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms (moderate SOE) and for CBT-M therapies over relaxation for PTSD symptoms (low SOE). Evidence also supports similar effectiveness for (1) CBT-exposure and EMDR for PTSD symptoms and (2) CBT-exposure and CBT-exposure plus cognitive restructuring (CR) for depression symptoms. The few head-to-head trials precluded the use of meta-analysis to pool the comparative effectiveness findings. Similarly, studies provided no evidence of the comparative effectiveness of interventions for other outcomes of interest such as anxiety symptoms, quality of life, disability or functional impairment, and return to work or active duty status.

The studies that met inclusion criteria provided insufficient strength of evidence regarding whether efficacy or effectiveness differed by patient characteristics or type of trauma exposure.

KQ 2. Pharmacological Treatments

Among the pharmacological treatments, we found moderate strength of evidence (SOE) supporting the efficacy of fluoxetine, paroxetine, and venlafaxine for PTSD symptoms. Prazosin, topiramate, olanzapine, risperidone, and sertraline also may have some benefit for PTSD symptoms (low SOE). Evidence was insufficient to determine whether other medications are efficacious for improving PTSD symptoms. Most of the medications with moderate evidence of efficacy had about a 10-point greater decrease in the CAPS assessment of PTSD symptoms at posttreatment compared with the inactive comparator group. Paroxetine and venlafaxine also had moderate SOE in support of remission and depression symptom decreases compared with the inactive comparator groups. Of note, fluoxetine and sertraline each found evidence of no difference on depression symptoms.

Table 30 summarizes the main findings and SOE for the pharmacological treatments with evidence of efficacy. The outcomes included in the table are those most commonly reported: PTSD symptoms, remission, and reduction of depression symptoms. Unlike the studies of psychological treatments, which often reported loss of PTSD diagnosis as an outcome,

pharmacological studies generally did not report it as an outcome. Similarly, studies mostly did not report evidence for other outcomes of interest such as anxiety symptoms, quality of life, disability or functional impairment, and return to work or active duty. Exceptions included evidence in support of the efficacy of fluoxetine and risperidone for anxiety symptoms (low SOE), efficacy of venlafaxine (moderate SOE) and sertraline (low SOE) for quality of life, and efficacy of paroxetine and venlafaxine for disability/functional impairment (moderate SOE).

Table 30. Summary of efficacy and strength of evidence of PTSD pharmacological treatments

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Fluoxetine (SSRI)	PTSD symptoms[a]	4 (835)[47, 61-63]	Reduced PTSD symptoms SMD -0.28 (95% CI -0.42 to -0.14)	Moderate
	Depression symptoms[b]	3 (771)[47, 61, 62]	Similar reduction in depression symptoms SMD -0.20 (95% CI -0.40 to 0.00)	Low SOE for no difference[c]
Paroxetine (SSRI)	PTSD symptoms[a]	2 (348)[64, 65]	Reduced PTSD symptoms SMD of -0.56 to -0.44 in individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
	PTSD symptom remission	2 (348)[64, 65]	Greater PTSD symptom reduction RD of 0.13 and 0.19 across 2 individual studies (1 of 2 studies p<0.05)	Moderate
	Depression symptoms[b]	2 (348)[64, 65]	Reduced depression symptoms SMD ranged from -0.60 to -0.34 across individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
Sertraline (SSRI)	PTSD symptoms[a]	7 (1,085)[66-72]	Reduced PTSD symptoms SMD -0.20 (95% CI -0.36 to -0.04)	Low[d]
	Depression symptoms[b]	7 (1,085)[66-72]	Similar reduction in depression symptoms SMD -0.14 (95% CI -0.33 to 0.06)	Low for no difference[e]
Venlafaxine (SNRI)	PTSD symptoms[a]	2 (687)[69, 73]	Reduced PTSD symptoms SMD of -0.35 and -0.26 across two individual studies	Moderate
	PTSD symptom remission	2 (687)[69, 73]	Greater PTSD symptom remission RD of 0.12 and 0.15 across individual studies	Moderate[f]
	Depression symptoms[b]	2 (687)[69, 73]	Reduced depression symptoms Between-group mean difference of -2.6 and -1.6 across two individual studies	Moderate[g]
Prazosin (alpha blocker)	PTSD symptoms[a]	3 (117)[74-76]	Reduced PTSD symptoms SMD -0.52 (95% CI, -0.90 to -0.14)	Low

Treatment	Symptom	N Trials (Subjects)	Findings	SOE
Topiramate (anticonvulsant)	PTSD symptoms[a]	3 (142)[77-79]	Reduced PTSD symptoms SMD range of -1.85 to -0.38 across individual studies	Low[h]
Olanzapine (antipsychotic)	PTSD symptoms[a]	2 (47)[80, 81]	Reduced PTSD symptoms SMD of -1.15 and -0.96 across individual studies,[80, 81] N=47	Low
		3 (62)[80-82]	SMD ranged from -1.15 to 0.89 across individual studies	
Risperidone (antipsychotic)	PTSD symptoms[a]	4 (422)[83-86]	Reduced PTSD symptoms SMD -0.26 (95% CI, -0.52 to -0.01)	Low

NOTE: Outcomes graded as insufficient are not included in this table. Insufficient evidence was provided for divalproex (anticonvulsant), tiagabine (anticonvulsant), citalopram (SSRI), all TCAs, buproprion (other SGA) and mirtazapine (other SGA). No studies that met inclusion criteria rated as having low or medium risk of bias evaluated lamotrigine (anticonvulsant), any benzodiazepine, desvenlafaxine (SNRI), duloxetine (SNRI), nefazodone (other SGA], or trazodone (other SGA).

[a] SMD from Clinician-Administered PTSD Scale and from various other PTSD symptom scales.
[b] SMD from the Beck Depression Inventory and from various other depression symptom scales.
[c] SOE changed from moderate in the prior review to low for no difference in the updated review. Only 2 of 3 studies favored treatment; one favored placebo. Imprecision, inconsistency, and effect sizes near the null prompted the change in grade.
[d] SOE changed from moderate in the prior review to low in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, and findings were imprecise.
[e] SOE changed from low to low for no difference in the updated review. The studies were inconsistent in whether findings favored treatment or the inactive comparator group, findings were imprecise, and most individual study estimates were close to the null.
[f] SOE changed from insufficient to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
[g] SOE changed from low to moderate in the updated review because of consistent evidence across two studies of adequate sample sizes.
[h] SOE changed from moderate in the prior review to low in the updated review. The findings were imprecise; only 1 of 3 individual studies found significant differences between study groups, and the sample sizes were small.

CI = confidence interval; N = number; PTSD = posttraumatic stress disorder; RD = risk difference; SMD = standardized mean difference; SNRI = serotonin and norepinephrine reuptake inhibitor; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

Little direct comparative evidence (i.e., head to head) was available to determine if pharmacological treatments differ in effectiveness. We identified just four medium risk of bias studies meeting inclusion criteria. Of those four, two compared medications that have evidence supporting their efficacy, sertraline and venlafaxine.[69, 186] Findings from these two studies provided limited evidence of no differences between groups for PTSD symptoms, quality of life, and disability (low SOE for no differences) and moderate evidence of no difference for depression (moderate SOE for no differences).

Our network meta-analysis of 33 trials included 13 active treatments (4,491 subjects) that reported CAPS-measured PTSD symptom outcomes to incorporate both direct and indirect evidence. No significant differences in effectiveness existed between the three medications with at least moderate SOE of efficacy for PTSD symptoms (fluoxetine, paroxetine, and venlafaxine). Of note, most of the evidence for these comparisons (as well as most comparisons made in the network meta-analysis) came from indirect comparisons because very few trials compared effectiveness between two interventions of interest.

The studies that met inclusion criteria provided insufficient strength of evidence regarding whether efficacy or effectiveness differed by patient characteristics or type of trauma exposure.

KQ 3. Psychotherapy Compared With Pharmacotherapy

We found just one study (N=88) that directly compared a psychological treatment (EMDR) with a pharmacological treatment (fluoxetine).[47] We concluded that the head-to-head evidence was insufficient, to draw any firm conclusions about comparative effectiveness because data were from a single, small study with medium risk of bias that provided imprecise findings of unknown consistency (insufficient SOE).

This study also provided insufficient strength of evidence regarding whether efficacy or effectiveness differed by patient characteristics or type of trauma exposure.

KQ 4. Adverse Events of Treatments

The included studies typically did not report the use of methods to systematically capture adverse event (AE) information collected by standardized measures such as a checklist. The few head-to-head trials that met inclusion criteria provided insufficient evidence to compare AEs across different interventions.

For psychological treatments, the majority of studies (76 of 93) reported no information about AEs. With such a small proportion of studies reporting data, the included psychological studies provided insufficient evidence to draw conclusions about withdrawals due to AEs, including serious AEs such as mortality; suicide; suicidal ideation; self-harmful behaviors; and other, nonserious specific AEs.

Studies that tested the efficacy and comparative effectiveness of pharmacological interventions generally lacked sufficient power to compare specific serious AEs such as mortality; suicidality; self-harmful behaviors; withdrawals due to AEs; and most of the other, nonserious AEs of interest between interventions (insufficient SOE due to high risk of bias, inconsistency or unknown consistency, lack of precision and low sample sizes). Placebo comparisons of specific AEs between pharmacological treatments graded as having at least moderate SOE of efficacy (fluoxetine, paroxetine, and venlafaxine) indicated small increased risk of a few AEs (Table 31). However, other systematic reviews of PTSD treatments have summarized AE evidence from studies of patients with other conditions such as depression, anxiety, and psychotic symptoms. For example, in studies of selective serotonin reuptake inhibitors/ serotonin and norepinephrine reuptake inhibitors for depression, frequently reported AEs include diarrhea (specifically for sertraline and venlafaxine), dizziness, dry mouth, fatigue, headache, nausea, sexual dysfunction, sweating, tremor, and weight gain; and paroxetine and venlafaxine appear to have greater discontinuation rates than placebo or other medications.[188, 189] Whether these findings apply to patients treated with these same medications for PTSD is unclear.

Limited evidence indicated higher rates of nausea, somnolence, and diarrhea for **fluoxetine** versus placebo (low SOE); nausea, dry mouth, and somnolence for **paroxetine** versus placebo (low SOE); and nausea (moderate SOE), dry mouth (low SOE), and constipation (low SOE) for **venlafaxine** versus placebo.

However, other systematic reviews of PTSD treatments have summarized AE evidence from studies of patients with other conditions such as depression, anxiety, and psychotic symptoms. For example, in studies of SSRIs/SNRIs for depression, frequently reported AEs include diarrhea (specifically for sertraline and venlafaxine), dizziness, dry mouth, fatigue, headache, nausea, sexual dysfunction, sweating, tremor, and weight gain; and paroxetine and venlafaxine appear to

Table 31. Risk difference and strength of evidence for selected adverse events with evidence of at least small risk (low strength of evidence) that compared pharmacological treatments to placebo[a]

Medication Class	Medication	Outcome	Results Risk Difference (95% CI)[b]	Strength of Evidence
SSRI	Fluoxetine	Nausea	0.03 and 0.07 in 2 individual trials; p=ns in both trials; N=712	Low
		Somnolence	0.04 and 0.06 (variation by dose of fluoxetine) in 1 trial; N=411; p=ns)	Low
		Diarrhea	0.24; 1 trial; N=44; p<0.05	Low
SSRI	Paroxetine	Nausea	0.11; 1 trial; N=323; p<0.05	Low
		Dry mouth	0.10; 1 trial; N=323; p<0.05	Low
		Somnolence	0.13; 1 trial; N=323; p<0.05	Low
SNRI	Venlafaxine ER	Nausea	0.10 in both individual trials; N=686; p<0.05 in both trials	Moderate
		Dry mouth	0.04 and 0.08 across 2 individual trials; N=686; significantly higher risk in 1 of 2 trials	Low
		Constipation	0.02 and 0.09 across 2 individual trials; N=686; significantly higher risk in 1 of 2 trials	Low

[a] Table includes only those pharmacological treatments with moderate SOE supporting its efficacy.
[b] Data reported are RDs between medications and placebo (95% CI; number of trials, number of subjects). These data are results of our RD calculations between groups. Positive RDs favor placebo (more events in the medication group).

Note: We did not include rows for adverse events with no data (i.e., those with zero included trials reporting data) or for intervention/outcome pairs with insufficient evidence of risk. The AEs included in the table are those reported by the included studies.

AE = adverse events; CI = confidence interval; ER = extended release; N = number; RD = risk difference; SNRI = serotonin and norepinephrine reuptake inhibitors; SOE = strength of evidence; SSRI = selective serotonin reuptake inhibitors.

have greater discontinuation rates than placebo or other medications.[188, 189] Whether these findings apply to patients treated with these same medications for PTSD is unclear.

Findings in Relation to What Is Already Known

Recent PTSD treatment guidelines have recommended several types of psychological and pharmacological treatments.[87, 88, 106] We also found evidence to support the efficacy of several psychological treatments and pharmacotherapies for adults with PTSD. Most notably, we found high SOE of efficacy for two psychological interventions, CBT-exposure and CBT-mixed therapies. For medication therapies, we found evidence of moderate efficacy for fluoxetine, paroxetine, and venlafaxine.

In general, these guidelines identify psychological treatments over pharmacological treatments as the preferred first-line treatment, with medication to be used adjunctively or as a second option when psychotherapy does not adequately decrease symptoms and associated impairment. These recommendations may have been made, in part, because of the presumed lower degree of potential harms associated with psychological treatments as compared with pharmacological treatments. Our review found a single study that tested a head-to-head psychological vs. pharmacological treatment (EMDR versus fluoxetine) but insufficient evidence to enable a conclusion on comparative effectiveness. Indirect evidence from our review might suggest that psychological treatments are more effective than pharmacological treatments, because effect sizes for reduction of PTSD symptoms are much larger in studies of the efficacious psychological treatments than in studies of the efficacious pharmacological treatments. However, conclusions based on indirect comparisons may be flawed when pooling data from different patient populations across individual studies from two different sets of literature (i.e., studies of psychological treatments and pharmacological treatments), and also

when comparators are not the same across studies (e.g., placebo pill versus wait-list). For example, differences in the severity of PTSD symptoms or functional impairment associated with PTSD across different studies may influence the outcomes.

Several existing guidelines and systematic reviews that have shown that some psychological therapies and some pharmacological treatments are effective treatments for adults with PTSD have recommended interventions similar to those found efficacious in the current review. The recently published American Psychological Association (APA) review found evidence to strongly recommend CPT, CT, CBT, PE, and, to a slightly lesser degree, recommend EMDR, NET, and BEP.[87] Each of these psychological treatments had at least moderate or high SOE of efficacy in the current review to reduce PTSD symptoms in this updated review, with the single exception of BEP, which has insufficient SOE for reduction in PTSD symptoms and low SOE for both loss of PTSD diagnosis and reduction in depression symptoms. The American Psychological Association group also recommended fluoxetine, paroxetine, venlafaxine, and sertraline, the same four medications recommended in the Department of Defense/Veterans Affairs guidelines;[88] this updated review found moderate SOE in support for fluoxetine, paroxetine, and venlafaxine as well, but limited evidence for sertraline (low SOE), driven by heterogeneity in individual study findings.

For the most part, the conclusions made in this update remain unchanged from our prior review published in 2013 on this topic.[89] Additional evidence prompted the increase of a few of the SOE grades for psychological treatments (e.g., CBT-mixed from moderate to high for reduction in PTSD symptoms, loss of PTSD diagnosis, and reduction in depression symptoms; CBT-exposure from moderate to high for loss of PTSD diagnosis; and EMDR from low to moderate for reduction in PTSD symptoms). Conversely, some of the SOE grades decreased from the last review for some of the pharmacological treatments after reassessing the SOE (fluoxetine from moderate to low for no difference for reduction in depression symptoms, sertraline from moderate to low for reduction in PTSD symptoms and from low to low for no difference for reduction in depression symptoms, and topiramate from moderate to low for reduction in PTSD symptoms), although SOE changed from insufficient to moderate for loss of PTSD diagnosis and low to moderate for reduction in depression symptoms for venlafaxine (reduction in PTSD symptoms remained at moderate). The SOE moved from insufficient to low for reduction in PTSD for four treatments—TAR, IRT, prazosin, and olanzapine. Consistent with the prior review, the evidence included in this update yielded mostly insufficient evidence regarding comparative effectiveness and harms associated with treatments of interest. Finally, our searches yielded no evidence of studies that met our inclusion/exclusion criteria that tested any of the newly added treatment types (energy psychology/emotional freedom techniques, and the three atypical antipsychotics—ziprasidone, aripiprazole, and quetiapine).

Applicability

Although patients enrolled in studies of psychological and pharmacological treatments included in our review tended to have similar patient characteristics, types of trauma exposure, and baseline severity of PTSD symptoms, studies may have recruited subjects from different settings (treatment versus community-based samples). In addition, different types of subjects may have been willing to enroll in psychological versus pharmacological treatment studies. For example, it is possible that more subjects enrolled in medication studies were "treatment-resistant" than those enrolled in psychological studies, after receiving various prior interventions that did not effectively treat their symptoms. Further, the study designs used for pharmacological

treatments could be considered more rigorous in some ways than psychological treatments (e.g., generally containing blinded patients and providers, which often is not possible with psychological treatments).

The studies included in this review generally enrolled subjects from outpatient settings who met criteria for clinical PTSD with severe levels of symptomatology. Thirteen of the studies, however, did not require all subjects to meet clinical PTSD diagnosis at study entry. Nevertheless, about two-thirds of the subjects in these 13 studies met clinical PTSD criteria. Entry to these studies, in the absence of a clinical diagnosis, generally depended on having a threshold level of symptoms from one or more existing scales. Therefore, some of the study findings from samples that included some subjects who did not meet clinical PTSD criteria may not generalize as well to adults with clinical PTSD. Because the studies included in this review all contained samples where at least half of the subjects met clinical criteria, we can conclude that the generalizability to all adults with PTSD was not greatly compromised. In fact, the findings are generally consistent between studies with samples that had less than 100% of subjects meeting clinical PTSD criteria versus samples that required a PTSD diagnosis at study entry.

Another potential factor affecting applicability has to do with variation across studies in the type, severity, chronicity, sequence, and/or combinations of trauma exposures experienced by study subjects prior to study entry. For one, studies inconsistently reported, and had wide variation in, the time between incident trauma and trial entry. The studies included a wide range of trauma exposures, and many enrolled a heterogeneous group of subjects with a variety of index trauma types. In addition, direct evidence was insufficient to determine whether findings are applicable to all of those with PTSD or whether they are applicable only to certain subgroups. Direct evidence of efficacy or comparative effectiveness across different subgroups of adults with PTSD also was insufficient. That is, from the evidence base collected for this review, we are unable to determine whether any treatment approaches are more or less effective for specific types of PTSD patients, including victims of particular types of trauma or those with comorbid conditions (see KQ 1a, 2a, and 3a).

Several interventions (primarily psychological) included in this review targeted those with comorbid PTSD and substance use disorders (SUDs)[20, 27, 56-58, 140, 145, 146, 149, 157] (one of which tested topiramate[165] and another which tested sertraline[67]), serious mental illness,[7] borderline personality disorder (BPD),[23, 144] depression,[145, 186] or psychosis.[16] Findings from these studies may not generalize to those who do not have the same comorbid disorder as the one required for inclusion. Also, some of the interventions were designed to address both PTSD and the co-occurring disorder of interest. For example, one of the interventions tested, Seeking Safety (SS), targets both PTSD and SUD symptoms; the studies testing SS each required SUD and PTSD diagnosis for study entry. Therefore, the applicability of SS for those without a comorbid SUD cannot be determined, as the findings from the SS studies herein only apply to those with comorbid conditions. On the flip side, because some studies excluded subjects with SUD, cognitive disorders, psychosis, suicidality, and/or serious medical comorbidities that tend to commonly occur in those with PTSD intervention, the findings from these studies may not apply to patients seen in clinical practice. In particular, because most pharmacological studies excluded persons who met criteria for alcohol or substance abuse or dependence either currently or within a specified time (typically 3-6 months) prior to study enrollment, findings from medication studies generally cannot be applied to those with substance use problems.

Implications for Clinical and Policy Decisionmaking

Despite evidence in support of the efficacy of several types of psychological and pharmacological treatments for PTSD, clinical uncertainty exists about what treatment to select for individual patients. As we noted in the previous review on this topic, practical considerations, such as presence or lack of availability of psychological treatments and patient preferences, may guide treatment decisions.[190] If numerous treatments are available and patients have no preference for a particular treatment, decisionmaking in the absence of sufficient direct evidence from head-to-head trials (including head-to-head psychological and pharmacological treatments) can be challenging. Additional studies that directly compare psychological to pharmacological treatments are needed to confirm or refute which treatments are truly more effective first-line treatments.

Nevertheless, choices must be made for patients in need of treatment. Given the findings, the magnitude of benefit and SOE found for CBT-exposure and CBT-mixed therapies support their use as helpful psychological treatments for PTSD. However, other factors must be considered in selecting a treatment for PTSD, including patient preference, access to and ability to pay for treatment, types of interventions tried previously with no difference, and clinical judgment about the appropriateness of an intervention given the presence of co-occurring disorders and severity and types of symptoms experienced. For example, a majority of the studies reviewed in this report excluded patients with presenting issues such as substance dependence or suicidality. Most clinicians would agree that stabilization of these issues should occur before initiating trauma-focused therapy.

If one decides to pursue treatment with a medication, paroxetine, venlafaxine, or fluoxetine may have the best evidence supporting efficacy. Studies provided evidence of moderate strength for each of these medications for PTSD symptoms and, for paroxetine and venlafaxine, remission, depression symptoms, and disability/functional impairment.

Limitations of the Comparative Effectiveness Review Process

The limitations of this update are similar to the limitations of the previous review. Specifically, the scope of this review was limited to studies that enrolled adults with PTSD. Separate reports have focused on children and adolescents.[191] We did not attempt to review literature on treatments for acute stress disorder or on interventions aimed to prevent PTSD for people exposed to trauma. Our review did not include an assessment of some factors important for clinical decision making, such as adherence or interactions with other therapies that could influence real world effectiveness of treatments. Further, we did not review literature on complementary and alternative medicine treatments.

Several newer studies that focused exclusively on sleep-related outcomes for trials targeting those with adult PTSD did not meet our review inclusion criteria. Some excluded studies did not meet our review inclusion criteria. Some excluded studies did not report between-group differences for one or more primary outcomes of interest (i.e., PTSD symptoms, remission, or loss of diagnosis), and outcomes of interest did not specifically include sleep disturbances, which frequently occur (and are part of the clinical criteria) among those with PTSD. Like other mental health problems, sleep plays a major role in PTSD-related functioning and outcomes. Future reviews might consider adding these important sleep-related outcomes to the inclusion criteria.

For KQs 1 through 3, we included randomized controlled trials (RCTs) with no sample size limit. We did not allow for inclusion of observational studies because observational studies that compare the effectiveness of various treatments for PTSD have a very high risk of selection bias and confounding. We believe that the results of such studies should not be used to make decisions about efficacy or effectiveness. For KQ 4, focused on harms, we allowed for observational studies to be included if they were prospective cohort studies or case-control studies with a sample size of 500 or greater. We did not find any observational study of this sample size or greater that otherwise met our inclusion criteria. The only studies providing information on harms were smaller studies with RCT designs.

For harms, useful information could possibly have been provided by studies conducted in other populations (i.e., those without PTSD). For example, many studies of some medications reviewed in this report enrolled patients with depression, anxiety, or psychotic disorders. Such studies may provide important information about adverse effects of the medications used to treat other conditions.

Our network meta-analysis used methods that do not rely solely on placebo-controlled trials; it allowed for the inclusion of data from head-to-head studies or those with active comparators. However, our network meta-analysis was limited almost entirely to indirect evidence because very few head-to-head trials were identified for inclusion. Therefore, findings of the network meta-analysis should be interpreted with caution, especially because of the heterogeneity in study samples, specific treatments tested, comparators, outcomes assessments, and timing of assessments. The validity of results derived from indirect comparisons requires careful interpretation because the characteristics cannot be assumed to be similar across studies.

Finally, publication bias and selective reporting are potential limitations. Although we searched for unpublished studies and unpublished outcomes, and did not find direct evidence of either of these biases, many of the included studies were published prior to the availability of trial registries (e.g., clinicaltrials.gov) that would allow for greater certainty in determining the potential for either type of bias.

Limitations of the Evidence Base

The evidence base was inadequate to draw conclusions for at least one of the main Key Questions and each of the subquestions of interest. As highlighted in the Key Findings and Strength of Evidence section, too few (and sometimes zero) studies with low- or medium-risk of bias were available to provide sufficient evidence regarding (1) whether some of the psychological and pharmacological treatments used to treat PTSD are efficacious; (2) comparative effectiveness of most of the treatments (including any of the psychological versus pharmacological interventions); (3) whether treatments differ in effectiveness for specific groups, such as those with different types of trauma or comorbid conditions; and (4) risk of most types of adverse effects for interventions of interest.

Among studies eligible for inclusion in this review, many more studies had high risk of bias (n=66) than low risk of bias (n=11) while the majority had medium risk of bias (n=116). We excluded the high risk of bias studies from our main data synthesis generally due to high or differential attrition coupled with inadequate methods for dealing with missing data and, less often, due to unblinded outcome assessors. Although the findings from the high risk of bias studies were generally consistent with those from low and medium risk of bias studies, removal of these studies reduced the precision of our analyses and ability to synthesize findings via meta-analysis. Nevertheless, removal of the high risk of bias studies was necessary in order to ensure

the validity and generalizability of our findings. The prior review, which conducted a quantitative sensitivity analysis to compare findings when including versus omitting high risk of bias studies, did not find appreciable differences in findings. Although high attrition rates in studies treating mental health conditions are not uncommon,[188, 189, 192] it is difficult to determine the reason for loss to followup (e.g., due to having more severe symptoms typical of PTSD such as avoidance and detachment or due to adverse effects associated with the treatment itself).

The heterogeneous nature of the samples of studies included in our review presented additional challenges. Differences in sample characteristics reduced the generalizability of findings and also precluded the ability to synthesize findings across studies with heterogeneous samples. Patient characteristics such as type of trauma exposure, severity of the exposure or symptoms experienced, time since trauma exposure/chronic versus acute exposure to trauma, as well as co-occurring mental or physical conditions decreased the applicability to those with similar characteristics. In addition, despite searching for evidence, we found very few investigations that examined whether efficacy or comparative effectiveness differs across these specific subgroups of adults with PTSD.

The treatment history of subjects enrolled in the studies also differed across study samples. Variation in how many prior treatments had been tried and whether the use of concurrent interventions were permitted further added to the heterogeneity of the evidence base.

The heterogeneous nature of the interventions within several categories further limits the evidence base. In particular, the studies in the CBT-M category varied widely in terms of combinations of components. Alternate strategies for categorizing the interventions, such as grouping psychotherapies into trauma-focused (TF) versus non-TF psychotherapies, were considered. Using this categorization, however, would require recategorization of studies across many different categories (e.g., CBT-exposure, CBT-mixed, EMDR) used in the prior review. If this schema was used to recategorize our current CBT-mixed group, only two studies[26, 27] of the 31 studies would be considered to be non-TF. Future reviews that focus on efficacy and effectiveness of PTSD treatments, however, might benefit from restructuring intervention grouping when synthesizing results and/or studying the individual components or combination of components that produce the most efficacy/effectiveness.

Descriptions of the comparators across treatments were often limited. In some cases, the distinction between treatments (if any) between subjects on a wait-list and those receiving usual care was not clear, as some subjects in a wait-list group also received treatment as usual. As a result, we combined these comparator groups into an “inactive comparator” group in our analyses to examine the efficacy of different interventions of interest.

The lack of followup data for many studies in this review also precludes the ability to conclude long-term efficacy or effectiveness. Pharmacological studies, in particular, tended to last from 8 to 12 weeks and not include a followup period. Relatedly, the timing of outcome assessments tended to vary much more widely for psychological than pharmacological interventions. Additional research would be needed to determine the impact that the timing of the posttreatment assessment has on outcomes.

Finally, our risk of bias assessment, which was done based on current recommendations,[193] did not account for the source of funding or allegiance of study authors may have impacted our findings. For example, some of our psychological intervention studies included the developer of the intervention as a study author (e.g., narrative exposure therapy[53, 54, 161] and brief eclectic psychotherapy).[50, 51] In addition, several of the drug trials were funded by the pharmaceutical companies that manufacture the medications tested.

Research Gaps

Our review highlights a number of research gaps that require additional investigations. Of note, these gaps specifically refer to the KQs included in this review; many other potential areas of research needed to address aspects of PTSD outside the scope of this review are not mentioned. Many of these gaps are highlighted in the Key Findings and Strength of Evidence section in the Results chapter and previously described in this chapter in the Limitations of the Evidence Base section. A summary of some of these gaps and suggestions for future research are noted in Table 32.

Table 32. Evidence gaps for future research, by Key Question

KQ	Evidence Gap	Potential Future Research
1	Most head-to-head evidence was insufficient to determine the comparative effectiveness of psychological treatments.	Future studies could focus on comparisons between the psychological treatments with at least moderate SOE supporting their efficacy (CPT, CT, CBT-exposure, CBT-mixed, EMDR, NET).
1	Evidence was insufficient to determine efficacy of some psychological treatments.	Future studies could evaluate promising therapies that have some evidence suggesting possible efficacy (e.g., trauma affect regulation, imagery rehearsal therapy, brief eclectic psychotherapy) or could evaluate new therapies that have not yet been studied but have some theoretical basis to support their potential efficacy or may be applicable to broader populations or to specific populations (e.g., those with particular comorbid conditions).
2	Most head-to-head evidence was insufficient to determine the comparative effectiveness of pharmacological treatments.	Future studies could focus on comparisons between the medications with moderate SOE supporting their effectiveness as compared with each other (fluoxetine, paroxetine, and venlafaxine).
2	Evidence was insufficient to determine efficacy of many medications.	Future studies could evaluate promising therapies that have some evidence suggesting possible efficacy (e.g., prazosin, topiramate, olanzapine, risperidone, sertraline) or could evaluate new therapies that have not yet been studied in trials meeting our inclusion/exclusion criteria (e.g., atypical antipsychotics ziprasidone, aripiprazole, or quetiapine).
3	Head-to-head evidence was insufficient to determine comparative effectiveness of psychological and pharmacological treatments.	Future studies could focus on comparisons between the psychological and pharmacological treatments with the best evidence of efficacy (e.g., paroxetine compared with CBT-exposure or CBT-mixed).
1a/2a/3a	Evidence was insufficient to make definitive conclusions about whether any treatment approaches are more efficacious or effective for patients with specific characteristics such as comorbid conditions or trauma exposure(s).	Future trials could include prespecified subgroup analyses to explore differences in efficacy or effectiveness for specific subgroups.
4	Studies with adequate sample sizes to detect significant differences in AEs across treatments.	Observational studies with sample sizes of 500 or more.
4	Studies with followup periods adequate to detect the occurrence of some AEs of interest,	Trials that include followups longer than 6 months' duration.
4	For psychological treatments, the majority of studies reported no information about AEs.	Future studies could include validated measures of AEs, including assessment of mortality, suicide, suicidal ideation, self-harmful behaviors, and hospitalizations.
4	For pharmacological treatments, few studies reported any information about withdrawals due to AEs, mortality, suicide attempts, suicidal ideation, self-harmful behaviors, or hospitalizations.	Future studies could include validated measures of AEs, including assessment of withdrawals due to AEs, mortality, suicide attempts, suicidal ideation, self-harmful behaviors, and hospitalizations.

KQ	Evidence Gap	Potential Future Research
4	For pharmacological treatments, most of the evidence for specific AEs was insufficient to determine whether the risk was increased, often primarily because of lack of precision.	Future studies could include validated measures of AEs to assess the risk of common AEs that might limit use of the medications (e.g., headache, gastrointestinal AEs, sexual AEs).
CQ	Components of effective psychological treatments (e.g., frequency or intensity of therapy and/or aspects of the therapeutic modality)?	Future studies could examine both components of effective treatments.
CQ	Fidelity of psychological interventions effective in trial settings when implemented in clinical practice settings.	Future studies could study the implementation of effective interventions in clinical practice settings and determine how fidelity influences the implementation.

Note: Within the gaps highlighted above, future research could address how various treatments compare for initial treatment and for treatment-refractory populations.

AE = adverse event; CBT = cognitive behavioral therapy; CPT = cognitive processing therapy; CQ = Contextual Question; CT = cognitive therapy; EMDR = eye movement desensitization and reprocessing; KQ = Key Question; NET = narrative exposure therapy; SOE = strength of evidence.

In addition to the evidence gaps noted here, several methodological improvements could be made to increase the validity of the findings. Although differences were slight, the changes in PTSD diagnostic criteria from DSM-IV to DSM-5 may influence the efficacy or effectiveness of certain interventions if samples only include those who met full criteria. Additional research is needed to determine if the changes in criteria have any impact on the outcomes of the interventions tested in this report (since most studies included used DSM-IV criteria to recruit participants). In addition, the continued application of methods designed to minimize attrition[194] and to appropriately account for missing data may help reduce the risk of bias inherent in many of these studies. Adding more followup assessments also may allow for the long-term benefits to be quantified. The use of systematic methods and reporting of AEs would increase the validity and reliability of harms assessment, which are important components used to weigh the risks and benefits associated with particular interventions. Testing comparative effectiveness using head-to-head trials, especially among interventions with demonstrated efficacy, may help guide treatment decisions. Finally, testing whether certain interventions work better for certain patient populations may help individualize care and increase the likelihood of treatment benefit.

Our lack of findings on each CQ suggests future research needs. First, additional studies are needed to understand the specific combinations or "doses" of components that may increase the likelihood of treatment effectiveness. Second, additional research is needed to explore the translation of clinical trial findings into practice.

Conclusions

Several psychological and pharmacological treatments have at least moderate SOE supporting their efficacy for adults with PTSD: CBT-exposure, CBT-mixed, CPT, CT, EMDR, NET, fluoxetine, paroxetine, and venlafaxine. Moderate SOE for the comparative effectiveness exists from head-to-head trials that favor CBT-exposure over relaxation therapy; evidence was insufficient to determine the comparative effectiveness of other treatments, including psychological and pharmacological treatment comparisons. Studies provided insufficient evidence to determine differences in the efficacy or comparative effectiveness of interventions by individual characteristics including comorbid condition and type, number, severity, or

chronicity of trauma exposure(s). Studies provided insufficient evidence about adverse events; no treatments had sufficient evidence of serious AE associations.

Appendix A. Intervention Descriptions

Table A-1. Psychological interventions used in treating PTSD

Intervention	Description
Cognitive behavioral therapy (CBT)	Uses principles of learning and conditioning to treat PTSD via individual or group therapy. It includes components from both behavioral and cognitive therapy. The therapist may use one or more components of CBT, including exposure, cognitive restructuring, and various coping skills to treat patients with PTSD. Most forms of CBT consist of a minimum of 8 to 12 weekly sessions lasting 60 to 90 minutes.[105, 108, 195, 196]
Cognitive interventions	Includes cognitive processing therapy (CPT), cognitive therapy (CT), and cognitive restructuring (CR). The theory behind cognitive interventions suggests that the interpretation of life events, rather than the event itself, determines an individual's mood. It aims to facilitate relearning thoughts and beliefs generated from a traumatic event, increase awareness of dysfunctional trauma-related thoughts, and correct or replace those thoughts with more adaptive or rational cognitions.[105, 108]
Coping skills therapy	Includes stress inoculation therapy (SIT), structured approach therapy, and relaxation training. All may use techniques such as education, muscle relaxation training, breathing retraining, and role playing to manage anxiety or correct misunderstandings conditioned at the time of trauma. The therapy is designed to increase coping skills for current situations. Most types of coping skills therapies require at least eight 60- to 90-minute sessions, while; more comprehensive interventions such as stress inoculation therapy require 10 to 14 sessions.[105, 108]
Exposure-based therapy	Involves confronting feared stimuli to extinguish the conditioned emotional response (usually anxiety) to traumatic stimuli. The therapist helps the client use mental imagery from memory or introduces hypothetical "scenes" of the traumatic event to the client (imaginal exposure). In some cases, the therapist uses an actual scene or similar events in life as the exposure (in vivo exposure).[101, 105, 108]
Eye movement desensitization and reprocessing (EMDR)	Combines imaginal exposure (described above) with the concurrent induction of rapid, intermittent eye movements believed to help reprogram brain function to resolve the emotional impact of trauma. In the EMDR process, the therapist instructs the patient to imagine a traumatic memory, engage in negative cognition, and articulate an incompatible positive cognition (e.g., personal worth). The therapist asks the patient to contemplate memory while focusing on rapid movement of the therapist's fingers. After 10 to 12 eye movements (back and forth), the therapist asks the patient to rate the strength of the memory and his or her belief in the positive cognition. Although earlier versions of EMDR consisted of one to three sessions, current standards consist of 8 to 12 90-minute weekly sessions.[108, 195]
Interpersonal therapy (IPT)	A time-limited, psychodynamic therapy that aims to alleviate patients' suffering and improve their interpersonal functioning. The premise of psychodynamic therapies assumes that PTSD symptoms result from unconscious memories, that the process of moving the memories into conscious awareness can allow the therapist to help the client work through thoughts about the memories. This type of therapy focuses specifically on interpersonal relationships and aims to help patients either improve their interpersonal relationships and social support, in part by changing their expectations about them.[197]
Trauma affect regulation (TAR)[a]	A manualized intervention designed to enhance the ability to anticipate and prevent or recover from (by regaining emotional equilibrium) the rapid acceleration of emotional distress associated with traumatic victimization.[59]
Narrative exposure therapy (NET)	A standardized, short-term treatment based on adapting CBT exposure therapy to meet the unique needs of those exposed to war and torture.[161]
Brief eclectic psychotherapy (BEP)	A manualized intervention that combines cognitive-behavioral and psychodynamic approaches for treating patients with PTSD. Eclectic psychotherapy uses techniques drawn from several different theoretical orientations. It allows flexibility in the approach the therapist uses in working with a patient to adapt to that individual's needs, rather than approaching the patient and his/her issues from a specific psychological orientation. Some therapists adhere largely to a single orientation, such as psychoanalysis or CBT but use eclectic techniques as needed. Other therapists self-identify as eclectic in orientation, using whichever techniques work best in any given situation. Number and length of sessions vary widely.

Intervention	Description
Imagery rehearsal therapy (IRT)	A therapy based on cognitive-behavioral "cognitive-behavioral technique" based on the notion that "waking activity can influence the content of night-time dreams."[156] IRT therapy targets trauma-related nightmares and, by doing so, attempts to reduce the severity of PTSD and improve the quality of sleep.
Memory specificity training (MEST)	A manualized treatment focused on decreasing faulty overgeneralization of memories. The goal is to improve problem solving and executive control by learning how to decrease cognitive avoidance and rumination. MEST can be performed using a 6 session (weekly) model or a 12 session biweekly model. Typically, sessions are 90 minutes in length.
Hypnosis	A technique for evoking a state of concentration that increases openness and ability to respond to suggestion and make changes to thoughts and behaviors. Often times used as an adjunct to other therapies and; it has been shown to significantly enhance efficacy of other treatments for many clinical conditions. Numbers and lengths of sessions vary widely.
Energy psychology including emotional freedom techniques (EFT)	A holistic method focused on the mind-body connectedness of thoughts, behaviors, sensations, and emotions. Techniques access energy systems via chakra techniques, biofield practices, and meridian interventions while administering psychological treatment. A related treatment, referred to as emotional freedom techniques (EFT), taps various energy points on the skin while focusing on various situations that evoke strong feeling, thoughts, or emotions to shift neurological pathways that facilitate improvements to psychological functioning.
Mindfulness based stress reduction (MBSR)	MBSR is a treatment that uses meditation to increase awareness of present mental and physical processes. The instructor leads participants through meditative exercises that focus on noticing sensations, thoughts, and emotions without judgment, and the participants practice short guided meditation exercises outside of sessions. Can be administered individually or in a group setting.
Neurofeedback training (NF)	NF is a type of biofeedback therapy where subjects respond to a display of their own brainwaves or other electrical activity of the nervous system to teach self-regulation of brain function in an effort to increase its efficiency. Sessions typically are administered over the course of several months.

[a] Full name: Trauma Affect Regulation: Guide for Education and Therapy (TARGET)

Table A-2. Pharmacological agents used in treating PTSD

Class	Drug
SSRIs	Citalopram, escitalopram, fluoxetine, fluvoxamine, paroxetine, and sertraline
SNRIs	Desvenlafaxine, venlafaxine, and duloxetine
TCAs	Imipramine, amitriptyline, and desipramine
Other second-generation antidepressants	Bupropion, mirtazapine, nefazodone, and trazodone
Alpha blockers	Prazosin
Second-generation (atypical) antipsychotics	Olanzapine, risperidone, ziprasidone, aripiprazole and quetiapine
Anticonvulsants (mood stabilizers)	Topiramate, tiagabine, lamotrigine, carbamazepine, and divalproex
Benzodiazepines	Alprazolam, diazepam, lorazepam, and clonazepam
Other medications	Naltrexone, cycloserine, and inositol

PTSD = posttraumatic stress disorder; SNRI = serotonin and norepinephrine reuptake inhibitors; SSRI = selective serotonin reuptake inhibitor; TCA = tricyclic antidepressant.

Appendix B. Outcome Measures and Instruments

Table B-1. Instruments used to measure outcomes of PTSD trials

Abbreviated Name	Complete Name	Description	Range/Meaning of Possible Scores	Improvement Indicated by
BDI	Beck Depression Inventory	21-item measure used to assess depression. Self-report or verbally administered by a trained professional administrator. Administration time approximately 5 minutes.	0 to 63	Decrease
CAPS	Clinician-Administered PTSD Scale	Current version includes a 30-item structured interview administered by a trained professional. Corresponds to the DSM-IV criteria for PTSD symptoms, impact on functioning, response validity, lifetime diagnosis, and overall PTSD severity. Time frame for assessment includes past week, month, or worst month since trauma. Administration time approximately 45 to 60 minutes. In the past there were different versions corresponding to different time periods. CAPS-1 (later renamed CAPS-DX) assessed current and lifetime PTSD diagnosis. The CAPS-2 (later renamed CAPS-SX) assessed the severity of symptoms over the past one week. These two versions were later combined into the current version, which can be used to assess either symptoms or diagnoses.	0 to136	Decrease
DTS	Davidson Trauma Scale	17-item self-report measure that assesses the 17 DSM-IV symptoms of PTSD. Each item corresponds to a DSM-IV symptom of PTSD, and each symptom is rated in terms of frequency and severity. Scores can be calculated for each of the 3 PTSD symptom clusters (B, C, and D). Administration time approximately 10 minutes.	0 to 136	Decrease
GAF	Global Assessment of Functioning	Clinician administered scale used to assess the social, occupational, and psychological functioning of adults.	0 to 100	Increase
HADS	Hospital Anxiety and Depression Scale	14-item self-report measure developed to assess anxiety and depression in non-psychiatric populations. Meant to differentiate symptoms of depression with those of anxiety. Administration time 5 minutes.	0 to 42	Decrease
HAM-A or HAS	Hamilton Anxiety Scale	14-item clinician administered measure used to assess the severity of anxiety symptoms. Administration time 10 to 15 minutes.	0 to 56	Decrease
HAM-D	Hamilton Depression Scale	17 or 21 item (depending on version) clinician administered scale used to measure the severity of depressive	0 to 54 (17 item)	Decrease

Abbreviated Name	Complete Name	Description	Range/Meaning of Possible Scores	Improvement Indicated by
		symptoms. Administration time 15 to 20 minutes.		
IES	Impact of Event Scale	15-item self-reported measure used to assess the frequency with which experiences of “intrusions,” “avoidance,” and emotional numbing related to stressful events occurred in the last week. A total distress score is calculated by summing all 15 item responses.	0 to 75	Decrease
IES-R	Impact of Events Scale-Revised	22-item self-report measure that assesses subjective distress caused by traumatic events. Contains 7 items more than the IES regarding hyperarousal symptoms of PTSD. Items correspond directly to 14 of the 17 DSM-IV symptoms of PTSD. Subscales can be computed for Intrusion, Avoidance, and Hyperarousal.	0 to 88	Decrease
MADRS	Montgomery-Asberg Depression Rating Scale	10-item clinician rated measure that assesses the severity of depression. Administration time approximately 15 minutes.	0 to 60	Decrease
MISS or M-PTSD	Mississippi Scale for Combat-related PTSD	35-item self-report questionnaire used to assess DSM-III combat-related PTSD and related features (depression, suicidality, and substance abuse). Administration time approximately 10 to 15minutes.	35 to 175	Decrease
MPSS-SR	Modified PTSD Symptom Scale	17-item self-report measure that assesses the 17 DSM-III-R symptoms of PTSD. Measure is a modification of the PTSD Symptom Scale (PSS). Major modifications are that items are not keyed to any particular traumatic event and that the MPSS-SR includes severity ratings in addition to the original measure’s frequency ratings for each item. It can be used to make a preliminary determination of the diagnosis of PTSD using either DSM-III-R criteria or a frequency, severity, or total score cutoff scores. It can be scored as a continuous measure of PTSD symptom severity.	0 to 68 (intensity) 0 to 51 (frequency)	Decrease
PTDS or PDS	Posttraumatic Diagnostic Scale	49- item self-report measure for severity of PTSD symptoms related to a single identified traumatic event. Assesses all DSM-IV criteria (A-F) in the past month (time frame can be adjusted). Four sections include: trauma checklist, description of post traumatic event, assessment of 17 PTSD symptoms, and interference of symptoms. Total severity score	0 to 51	Decrease

Abbreviated Name	Complete Name	Description	Range/Meaning of Possible Scores	Improvement Indicated by
		reflecting frequency of 17 PTSD symptoms.		
PCL	PTSD Checklist	17-item self-report measure of the 17 DSM-IV symptoms of PTSD. Has been used to screen individuals for PTSD, diagnose PTSD, and monitor symptom change during and after treatment. There are three versions of the PCL: PCL-M (military), PCL-C (civilian), and PCL-S (specific). Administration time approximately 5 to10 minutes.	17 to 85	Decrease
PTSD-I	PTSD Interview	Structured clinical interview. Patients given a copy of scale to read along with interviewer and asked to give subjective ratings for each symptom.		Decrease
PSS-I	PTSD Symptom Scale Interview	17-item semistructured interview that assesses the presence and severity of DSM-IV PTSD symptoms related to a single identified traumatic event in individuals with a known trauma history. Each item is assessed with a brief, single question. Interviewees are asked about symptoms they have experienced in the past 2 weeks. Administration time approximately 20 minutes.	0 to 51	Decrease
PSS-SR	PTSD Symptom Scale Self-report Version	17-item self-report scale used to diagnose PTSD according to DSM-III-R criteria. Assesses the severity of PTSD symptoms (consists of the same 17 items as the PSS-I).	0 to 51	Decrease
Q-LES-Q-SF	Quality of Life Enjoyment and Satisfaction Questionnaire-Short Form	16-item self-report questionnaire that assesses overall enjoyment and satisfaction with physical health, mood, work, household and leisure activities, social and family relationships, daily functioning, sexual life, economic status, overall well-being and medications.	14 to 70	Increase
SF-36	36-Item Short Form Health Survey	36-item scale of patient health status. Administrating time less than 15 minutes	0 to 100 (mean)	Increase
SI-PTSD or SIP	Structured Interview for PTSD	Assesses the 17 PTSD symptoms as well as survival and behavioral guilt. For each item, the interviewer assigns a severity rating that reflects both frequency and intensity. Responses can be used to make a determination about whether client's symptoms meet DSM criteria B, C, and D for PTSD. Administration time approximately 20 to 30 minutes.	0 to 68	Decrease

Abbreviated Name	Complete Name	Description	Range/Meaning of Possible Scores	Improvement Indicated by
SCID	Structured Clinical Interview PTSD Module	Semistructured interview used to assess the prevalence, absence, and subthreshold presence of PTSD used across trauma populations. Consists of separate modules corresponding to categories of diagnoses. Administration time 25 minutes.	Not quantitatively scored	Decrease
SCL-90-R	Symptom Checklist-90-Revised	90-item self-report questionnaire used to assess a broad range of psychological problems, symptoms of psychopathology, patient progress, and treatment outcomes. Administration time approximately 12 to15 minutes.	0 to 360	Decrease
SDS	Sheehan Disability Scale	5-item self-report measure developed to assess functional impairment in work/school, social and family life.	0 to 30	Decrease
SF-12	Medical Outcome Study Self-Report Form	12-item self-report measure of overall health status. Administrating time less than 15 minutes.	0 to 100	Increase
SPRINT	Short PTSD Rating Interview	8-item self-report measure that assesses the core symptoms of PTSD (intrusion, avoidance, numbing, arousal), somatic malaise, stress vulnerability, and role and social functional impairment.	0 to 32	Decrease
STAI	State-Trait Anxiety Inventory	20-item self-report measure that assesses state and trait anxiety. Administration time approximately 10 to 20 minutes.	20 to 80	Decrease
TOP-8	Treatment-Outcome Post-Traumatic Stress Disorder Scale	8-item measure based on all three symptom clusters of post-traumatic stress disorder.	0 to 32	Decrease
WAS	Work and Social Adjustment Scale	5-item measure of general social impairment.	0 to 40	Decrease

Appendix C. Search Strategy

4/24/17 PubMed

Search	Query	Items found
#1	Search ("Stress Disorders, Post-Traumatic"[Mesh] OR "post-traumatic stress disorder"[All Fields] OR "post-traumatic stress disorders"[All Fields] OR “posttraumatic stress disorder”[All Fields] OR “posttraumatic stress disorders”[All Fields] OR (disorder* AND "post-traumatic"[tiab]) OR "Stress Disorders, Traumatic"[Mesh:NOEXP] OR "Combat Disorders"[Mesh] OR PTSD OR "stress disorder"[All Fields] OR "traumatic event"[All Fields] OR "traumatic incident"[All Fields]	38936
#2	Search ("implosive therapy"[MeSH Terms] OR "implosive therapy"[All Fields] OR ("exposure"[tiab] AND ("therapy"[tiab] OR "psychotherapy"[tiab])) OR “imaginal exposure” OR “Biofeedback, Psychology”[Mesh] OR biofeedback or neurofeedback OR “Relaxation Therapy”[Mesh] OR “relaxation training”[All Fields] OR “cognitive therapy”[MeSH] OR cognitive restructur*[tiab] OR cognitive processing therap*[tiab] OR "Adaptation, Psychological"[Mesh] OR coping skill*[tiab] OR "stress inoculation" OR “assertiveness training” OR (psychodynamic[All Fields] AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields])) OR (psychodynamic[All Fields] AND ("psychotherapy"[MeSH Terms] OR "psychotherapy"[All Fields])) OR (("psychoanalytic"[All Fields] AND "psychotherapy"[All Fields]) OR "psychoanalytic psychotherapy"[All Fields]) OR (("psycho-analytic"[All Fields] AND "psychotherapy"[All Fields]) OR "psycho-analytic psychotherapy"[All Fields]) OR (("psycho-analytic"[All Fields] AND "psychotherapy"[All Fields]) OR "psycho-analytic psychotherapy"[All Fields]) OR "psychoanalytic therapy" OR "psycho-analytic therapy" OR “Eye Movement Desensitization Reprocessing”[MeSH] OR "EMDR"[tiab] OR "Psychotherapy"[Mesh] OR “brief eclectic psychotherapy” OR "interpersonal therapy” OR “interpersonal psychotherapy” OR "family therapy"[tiab] OR "marital therapy"[tiab] OR “group therapy” OR “group psychotherapy” OR “group psychological therapy” OR "Hypnosis"[Mesh] OR hypnotherapy OR "eclectic psychotherapy"[All Fields]	317456
#3	Search (#1 and #2)	8489
#4	Search ("Benzodiazepines"[Mesh] OR "Antidepressive Agents, Tricyclic"[Pharmacological Action] OR "Anticonvulsants"[Pharmacological Action] OR "Adrenergic alpha-Antagonists"[Pharmacological Action] OR "Antipsychotic Agents"[Pharmacological Action] OR "Antidepressive Agents"[Pharmacological Action])	432895
#5	Search ("Serotonin Uptake Inhibitors"[Mesh] OR "Serotonin Uptake Inhibitors" [Pharmacological Action] OR "Serotonin and Noradrenaline Reuptake Inhibitors"[Mesh] OR SSRI* OR SNRI* OR "citalopram” OR “escitalopram” OR “fluoxetine” OR “fluvoxamine” OR “paroxetine” OR “sertraline” OR “desvenlafaxine” OR “venlafaxine” OR “duloxetine” OR “imipramine” OR “amitriptyline” OR “desipramine” OR “bupropion” OR “mirtazapine” OR “nefazodone” OR “trazodone” OR “prazosin” OR “olanzapine” OR “risperidone” OR “benzodiazepines” [MeSH] OR “alprazolam” OR “diazepam” OR “lorazepam” OR “clonazepam” OR “topiramate” OR “tiagabine” OR “lamotrigine” OR “carbamazepine” OR “divalproex”)	175887
#6	Search (#4 or #5)	464165
#7	Search (#1 and #6)	1696
#8	Search (#3 or #7)	9804
#9	Search (#3 or #7) Filters: Humans	9065
#10	Search (#3 or #7) Filters: Humans; English	8375
#11	Search (#3 or #7) Filters: Humans; English; Adult: 19+ years	4920
#12	Search (#11 NOT (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt]))	4780
#13	Search (((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]) OR (controlled[title/abstract] AND trial[title/abstract]) OR "controlled clinical trial"[publication type] OR "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]))	669168
#14	Search (#12 and #13)	861

Search	Query	Items found
#15	Search ("Comparative Study"[Publication Type] OR "comparative study" OR "case control study"[all fields] OR "case control studies"[all fields] OR "Case-Control Studies"[Mesh] OR "Cohort Studies"[Mesh] OR “cohort effect”[MeSH Term] OR cohort*[tiab] OR “prospective studies”[MeSH] OR ((prospective*[All Fields] AND cohort[All Fields] AND (study[All Fields] OR studies[All Fields])))	3449493
#16	Search (#12 and #15)	1479
#17	Search (#14 or #16)	1997
#18	Search (#14 or #16) Filters: Publication date from 2012/01/01 to 2017/12/31	690
#19	Search (("review"[Publication Type] AND "systematic"[tiab]) OR "systematic review"[All Fields] OR ("review literature as topic"[MeSH AND "systematic"[tiab]) OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields])	202604
#20	Search (#12 and #19)	67
#21	Search (#12 and #19) Filters: Publication date from 2012/01/01 to 2017/12/31	38
#22	Search (“energy psychology”[All Fields] OR EFT OR “emotional freedom technique”[All Fields] OR "Monoamine Oxidase Inhibitors"[Mesh] OR "Naltrexone"[Mesh] OR "Cycloserine"[Mesh] OR "Adrenergic alpha-Antagonists"[Mesh] OR “Alpha blocker”[All Fields] OR “Alpha blockers”[All Fields] OR Olanzapine OR Risperidone OR Ziprazidone OR “mood stabilizer” [All Fields] OR “mood stabilizers” [All Fields] OR "Antidepressive Agents, Second-Generation"[Mesh] OR “second-generation antidepressants”[All Fields] OR “atypical antipsychotics” OR "Aripiprazole"[Mesh] OR Aripiprazole OR "Quetiapine Fumarate"[Mesh] OR Quetiapine)	66082
#23	Search (#1 and #22)	518
#24	Search (#1 and #22) Filters: Humans	435
#25	Search (#1 and #22) Filters: Humans; English	419
#26	Search (#1 and #22) Filters: Humans; English; Adult: 19+ years	242
#27	Search (#26 NOT (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt]))	212
#28	Search (#27 and (#13 or #15))	121
#29	Search (#27 and #19)	4

4/24/17 Cochrane Library

ID	Search	Hits
#1	[mh "Stress Disorders, Post-Traumatic"] or "post-traumatic stress disorder" or "post-traumatic stress disorders" or "posttraumatic stress disorder" or "posttraumatic stress disorders" or (disorder* and "post-traumatic") or [mh ^"Stress Disorders, Traumatic"] or [mh "Combat Disorders"] or PTSD or "stress disorder" or "traumatic event" or "traumatic incident"	3451
#2	[mh "implosive therapy"] or "implosive therapy" or (exposure and (therapy or psychotherapy)) or "imaginal exposure" or [mh "Biofeedback, Psychology"] or biofeedback or neurofeedback or [mh "Relaxation Therapy"] or "relaxation training" or [mh "cognitive therapy"] or cognitive restructur* or cognitive processing therap* or [mh "Adaptation, Psychological"] or coping skill* or "stress inoculation" or "assertiveness training" or (psychodynamic and ([mh /TH] or therapy or [mh therapeutics] or therapeutics)) or (psychodynamic and ([mh psychotherapy] or psychotherapy)) or (psychoanalytic and psychotherapy) or "psychoanalytic psychotherapy" or ("psycho-analytic" and psychotherapy) or "psycho-analytic psychotherapy" or "psychoanalytic therapy" or (psychoanalytic and therapy) or (psycho-analytic and therapy) or [mh "Eye Movement Desensitization Reprocessing"] or EMDR or [mh Psychotherapy] or "brief eclectic psychotherapy" or "interpersonal therapy" or "interpersonal psychotherapy" or "family therapy" or "marital therapy" or "group therapy" or "group psychotherapy" or "group psychological therapy" or [mh Hypnosis] or hypnotherapy or "eclectic psychotherapy"	42426
#3	#1 and #2	1504
#4	[mh Benzodiazepines] or [mh "Antidepressive Agents, Tricyclic"] or "tricyclic antidepressants" or [mh Anticonvulsants] or anticonvulsants or [mh "Adrenergic alpha-Antagonists"] or "adrenergic alpha-antagonists" or "Antipsychotic Agents" or antipsychotics or "Antidepressive Agents"	22306
#5	[mh "Serotonin Uptake Inhibitors"] or "Serotonin Uptake Inhibitors" or [mh "Serotonin and Noradrenaline Reuptake Inhibitors"] or SSRI or SSRIs or SNRI or SNRIs or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or desvenlafaxine or venlafaxine or duloxetine or imipramine or amitriptyline or desipramine or bupropion or mirtazapine or nefazodone or trazodone or prazosin or olanzapine or risperidone or [mh Benzodiazepines] or alprazolam or diazepam or lorazepam or clonazepam or topiramate or tiagabine or lamotrigine or carbamazepine or divalproex	34756
#6	#4 or #5	41927
#7	#1 and #6	567
#8	#3 or #7	1878
#9	Adult*:ti,ab,kw or [mh Adult]	441121
#10	#8 and #9	1109
#11	#10 not (letter:pt or newspaper article:pt or editorial:pt or comment:pt) Publication Year from 2012 to 2017	635
#12	"energy psychology" or EFT or "emotional freedom technique" or [mh "Monoamine Oxidase Inhibitors"] or [mh Naltrexone] or [mh Cycloserine] or [mh "Adrenergic alpha-Antagonists"] or "Alpha blocker" or "Alpha blockers" or Olanzapine or Risperidone or Ziprazidone or "mood stabilizer" or "mood stabilizers" or [mh "Antidepressive Agents, Second-Generation"] or "second-generation antidepressants" or "atypical antipsychotics" or [mh Aripiprazole] or Aripiprazole or [mh "Quetiapine Fumarate"] or Quetiapine	10593
#13	#1 and #12	182
#14	#13 and #9	110
#15	#14 not #11	66

4/24/17 CINAHL (Cumulative Index to Nursing and Allied Health)

#	Query	Limiters/Expanders	Last Run Via	Results
S1	(MH "Stress Disorders, Post-Traumatic") or "post-traumatic stress disorder" or "post-traumatic stress disorders" or "posttraumatic stress disorder" or "posttraumatic stress disorders" or (disorder* and "post-traumatic") OR "Combat Disorders" or PTSD or "stress disorder" or "traumatic event" or "traumatic incident"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	18,308
S2	"implosive therapy" or (exposure and (therapy or psychotherapy)) or "imaginal exposure" or biofeedback or neurofeedback or "Relaxation Therapy" or "relaxation training" or "cognitive therapy" or cognitive restructur* or cognitive processing therap* or "Adaptation, Psychological" OR “psychological adaptation” or coping skill* or "stress inoculation" or "assertiveness training" or (psychodynamic and (therapy or therapeutics)) or (psychodynamic and psychotherapy) or (psychoanalytic and psychotherapy) or "psychoanalytic psychotherapy" or ("psycho-analytic" and psychotherapy) or "psycho-analytic psychotherapy" or "psychoanalytic therapy" or (psychoanalytic and therapy) or (psycho-analytic and therapy) or "Eye Movement Desensitization Reprocessing" or EMDR or Psychotherapy or "brief eclectic psychotherapy" or "interpersonal therapy" or "interpersonal psychotherapy" or "family therapy" or "marital therapy" or "group therapy" or "group psychotherapy" or "group psychological therapy" or Hypnosis or hypnotherapy or "eclectic psychotherapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	83,975
S3	S1 AND S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3,387
S4	(MH "Antianxiety Agents, Benzodiazepine") or (MH "Antidepressive Agents, Tricyclic") or "tricyclic antidepressants" or anticonvulsants or (MH "Adrenergic alpha-Antagonists") or "adrenergic alpha-antagonists" or "Antipsychotic Agents" or antipsychotics or "Antidepressive Agents"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	34,533
S5	(MH "Serotonin Uptake Inhibitors") or "Serotonin Uptake Inhibitors" or "Noradrenaline Reuptake Inhibitors" or SSRI or SSRIs or SNRI or SNRIs or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or desvenlafaxine or venlafaxine or duloxetine or imipramine or amitriptyline or desipramine or bupropion or mirtazapine or nefazodone or trazodone or prazosin or olanzapine or risperidone or alprazolam or diazepam or lorazepam or clonazepam or topiramate or tiagabine or lamotrigine or carbamazepine or divalproex	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	22,091

#	Query	Limiters/Expanders	Last Run Via	Results
S6	S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	48,416
S7	S1 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	569
S8	S3 OR S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3,772
S9	S8	Limiters - Published Date: 20120101-20171231; English Language; Exclude MEDLINE records; Human; Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	248
S10	S9	Limiters - Publication Type: Clinical Trial, Randomized Controlled Trial Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	14
S11	S9	Limiters - Publication Type: Meta-Analysis, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	24
S12	"comparative study" OR (MH “comparative studies”) OR "case control study" OR (MH "case control studies") OR “Cohort Study” OR "Cohort Studies" OR “cohort effect” OR cohort* OR (MH “prospective studies”) OR ((prospective* AND cohort AND (study OR studies))	Limiters - Publication Type: Meta-Analysis, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	4,940
S13	S9 AND S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	1

#	Query	Limiters/Expanders	Last Run Via	Results
S14	"energy psychology" or EFT or "emotional freedom technique" or (MH "Monoamine Oxidase Inhibitors") or Naltrexone or Cycloserine or "Alpha blocker" or "Alpha blockers" or Olanzapine or Risperidone or Ziprazidone or "mood stabilizer" or "mood stabilizers" or (MH "Antidepressive Agents, Second-Generation") or "second-generation antidepressants" or "atypical antipsychotics" or Aripiprazole or Quetiapine	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	8,996
S15	S1 AND S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	118
S16	S15 NOT (S10 OR S11 OR S13)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	115
S17	S16	Limiters - English Language; Exclude MEDLINE records; Human; Age Groups: Adult: 19-44 years Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	2

4/24/17 PsycINFO

#	Query	Limiters/Expanders	Last Run Via	Results
S1	(DE "Post-Traumatic Stress") OR "post-traumatic stress disorder" OR "post-traumatic stress disorders" OR “posttraumatic stress disorder” OR “posttraumatic stress disorders” OR (disorder* AND "post-traumatic") OR “Combat Disorder” OR "Combat Disorders” OR PTSD OR "stress disorder" OR "traumatic event" OR "traumatic incident"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	45,098
S2	(DE "implosive therapy") OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR “imaginal exposure” OR (DE “Biofeedback, Psychiatry”) OR biofeedback or neurofeedback OR (DE “Relaxation Therapy”) OR “relaxation training” OR (DE “cognitive therapy”) OR cognitive restructur* OR “cognitive processing therapy” OR “Psychological Adaptation” OR coping skill* OR "stress inoculation" OR “assertiveness training” OR (DE “Psychodynamic Psychotherapy) OR (psychodynamic AND ("therapy" OR "therapeutics")) OR (psychodynamic AND "psychotherapy") OR ("psychoanalytic" AND "psychotherapy") OR "psychoanalytic psychotherapy" OR ("psycho-analytic" AND "psychotherapy”) OR "psycho-analytic psychotherapy" OR "psychoanalytic therapy" OR "psycho-analytic therapy" OR (DE “Eye Movement Desensitization Therapy”) OR “eye movement desensitization reprocessing” OR EMDR OR (DE "Psychotherapy") OR “brief eclectic psychotherapy” OR "interpersonal therapy” OR “interpersonal psychotherapy” OR "family therapy" OR "marital therapy" OR “group therapy” OR “group psychotherapy” OR “group psychological therapy” OR Hypnosis OR hypnotherapy OR "eclectic psychotherapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	56,231
S3	S1 AND S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	3,999
S4	(DE "Benzodiazepines") OR (DE “Antidepressant Drugs”) OR "Tricyclic Antidepressive Agents" OR (DE Tricyclic Antidepressant Drugs”) OR (DE “Anticonvulsive Drugs”) OR Anticonvulsants OR "Adrenergic alpha-Antagonists" OR (DE “Neuroleptic Drugs”) OR "Antipsychotic Agents"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	26,309

#	Query	Limiters/Expanders	Last Run Via	Results
S5	"Serotonin Uptake Inhibitors" OR (DE "Serotonin and Norepinephrine Reuptake Inhibitors") OR SSRI* OR SNRI* OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines [MeSH] OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	52,931
S6	S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	66,322
S7	S1 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1,129
S8	S7	Limiters - Publication Year: 2012-2017; English; Age Groups: Adulthood (18 yrs & older); Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	148
S9	S8	Limiters - Methodology: CLINICAL CASE STUDY, CLINICAL TRIAL, EMPIRICAL STUDY, - Experimental Replication, - Followup Study, -Longitudinal Study, ---Prospective Study, ---Retrospective Study, QUALITATIVE STUDY, QUANTITATIVE STUDY, TREATMENT OUTCOME Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	136
S10	S8	Limiters - Methodology: - Systematic Review, META ANALYSIS Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1

#	Query	Limiters/Expanders	Last Run Via	Results
S11	“energy psychology” OR EFT OR “emotional freedom technique” OR (DE "Monoamine Oxidase Inhibitors”) OR Naltrexone OR Cycloserine OR "Adrenergic alpha-Antagonists" OR “alpha blocker” OR “alpha blockers” OR Olanzapine OR Risperidone OR Ziprazidone OR (DE “Mood Stabilizers”) OR “mood stabilizer” OR “mood stabilizers” OR “second-generation antidepressants”[All Fields] OR “atypical antipsychotics” OR Aripiprazole OR Quetiapine	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	25,549
S12	S1 AND S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	409
S13	S12	Limiters - English; Language: English; Age Groups: Adulthood (18 yrs & older); Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	173
S14	S13	Limiters - Methodology: CLINICAL CASE STUDY, CLINICAL TRIAL, EMPIRICAL STUDY, - Experimental Replication, - Followup Study, -Longitudinal Study, ---Prospective Study, ---Retrospective Study, QUALITATIVE STUDY, QUANTITATIVE STUDY, TREATMENT OUTCOME Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	157
S15	S13	Limiters - Methodology: - Systematic Review, META ANALYSIS Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1

4/24/17 Published International Literature on Traumatic Stress (PILOTS)

Set#	Searched for	Databases	Results
S1	("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	35806
S2	SU.EXACT("Adults") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	22537
S3	(("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	16050
S4	("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	11434

Set#	Searched for	Databases	Results
S5	((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	3416
S6	("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex) AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	1332

Set#	Searched for	Databases	Results
S7	((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex) AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	510

Set#	Searched for	Databases	Results
S8	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex) AND la.exact("English")))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	3838

Set#	Searched for	Databases	Results
S9	("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	5458

S10	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex) AND la.exact("English")))) AND (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	1187

Set#	Searched for	Databases	Results
	outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English"))		
S11	("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English") AND pd(20120101-20171231)	PILOTS: Published International Literature On Traumatic Stress	1850
S12	("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English") AND pd(20120101-20171231)	PILOTS: Published International Literature On Traumatic Stress	546

Set#	Searched for	Databases	Results
S13	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex) AND la.exact("English")))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English") AND pd(20120101-20171231))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	45

Set#	Searched for	Databases	Results
S15	("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	354
S16	((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	127
S17	("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	5458

Set#	Searched for	Databases	Results
S18	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	80
S19	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English"))) NOT (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English") AND pd(20120101-20171231))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	42

Set#	Searched for	Databases	Results
S20	("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	1142
S21	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	6

S22	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English"))) NOT ((((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	1

Set#	Searched for	Databases	Results
	drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex) AND la.exact("English")))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English") AND pd(20120101-20171231)))		

Set#	Searched for	Databases	Results
S23	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND SU.EXACT("Adults")) AND ("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy")) OR ((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND SU.EXACT("Adults")) AND ("benzodiazepine derivatives" or "tricyclic derivatives" or "antimanic drugs" or anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" or "antiadrenergic agents" or "antipsychotic drugs" or "antiadrenergic agents" or "antidepressant drugs" or "antiadrenergic agents" or “antidepressant drugs" or "antiadrenergic agents" or citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex))) AND ("randomized clinical trial" or "single-blind" or "double-blind" or "random allocation" or "comparative study" OR case control stud* or "cohort studies" OR "cohort effect" OR cohort* or trial or "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR “prospective studies”) AND pd(20120101-20171231)	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	529

9/29/17 PubMed

Search	Query	Items found
#1	Search ("Stress Disorders, Post-Traumatic"[Mesh] OR "post-traumatic stress disorder"[All Fields] OR "post-traumatic stress disorders"[All Fields] OR “posttraumatic stress disorder”[All Fields] OR “posttraumatic stress disorders”[All Fields] OR (disorder* AND "post-traumatic"[tiab]) OR "Stress Disorders, Traumatic"[Mesh:NOEXP] OR "Combat Disorders"[Mesh] OR PTSD OR "stress disorder"[All Fields] OR "traumatic event"[All Fields] OR "traumatic incident"[All Fields]	40322
#2	Search ("implosive therapy"[MeSH Terms] OR "implosive therapy"[All Fields] OR ("exposure"[tiab] AND ("therapy"[tiab] OR "psychotherapy"[tiab])) OR “imaginal exposure” OR “Biofeedback, Psychology”[Mesh] OR biofeedback or neurofeedback OR “Relaxation Therapy”[Mesh] OR “relaxation training”[All Fields] OR “cognitive therapy”[MeSH] OR cognitive restructur*[tiab] OR cognitive processing therap*[tiab] OR "Adaptation, Psychological"[Mesh] OR coping skill*[tiab] OR "stress inoculation" OR “assertiveness training” OR (psychodynamic[All Fields] AND ("therapy"[Subheading] OR "therapy"[All Fields] OR "therapeutics"[MeSH Terms] OR "therapeutics"[All Fields])) OR (psychodynamic[All Fields] AND ("psychotherapy"[MeSH Terms] OR "psychotherapy"[All Fields])) OR (("psychoanalytic"[All Fields] AND "psychotherapy"[All Fields]) OR "psychoanalytic psychotherapy"[All Fields]) OR (("psycho-analytic"[All Fields] AND "psychotherapy"[All Fields]) OR "psycho-analytic psychotherapy"[All Fields]) OR (("psycho-analytic"[All Fields] AND "psychotherapy"[All Fields]) OR "psycho-analytic psychotherapy"[All Fields]) OR "psychoanalytic therapy" OR "psycho-analytic therapy" OR “Eye Movement Desensitization Reprocessing”[MeSH] OR "EMDR"[tiab] OR "Psychotherapy"[Mesh] OR “brief eclectic psychotherapy” OR "interpersonal therapy” OR “interpersonal psychotherapy” OR "family therapy"[tiab] OR "marital therapy"[tiab] OR “group therapy” OR “group psychotherapy” OR “group psychological therapy” OR "Hypnosis"[Mesh] OR hypnotherapy OR "eclectic psychotherapy"[All Fields]	323283
#3	Search (#1 and #2)	8733
#4	Search ("Benzodiazepines"[Mesh] OR "Antidepressive Agents, Tricyclic"[Pharmacological Action] OR "Anticonvulsants"[Pharmacological Action] OR "Adrenergic alpha-Antagonists"[Pharmacological Action] OR "Antipsychotic Agents"[Pharmacological Action] OR "Antidepressive Agents"[Pharmacological Action])	436720
#5	Search ("Serotonin Uptake Inhibitors"[Mesh] OR "Serotonin Uptake Inhibitors" [Pharmacological Action] OR "Serotonin and Noradrenaline Reuptake Inhibitors"[Mesh] OR SSRI* OR SNRI* OR "citalopram” OR “escitalopram” OR “fluoxetine” OR “fluvoxamine” OR “paroxetine” OR “sertraline” OR “desvenlafaxine” OR “venlafaxine” OR “duloxetine” OR “imipramine” OR “amitriptyline” OR “desipramine” OR “bupropion” OR “mirtazapine” OR “nefazodone” OR “trazodone” OR “prazosin” OR “olanzapine” OR “risperidone” OR “benzodiazepines” [MeSH] OR “alprazolam” OR “diazepam” OR “lorazepam” OR “clonazepam” OR “topiramate” OR “tiagabine” OR “lamotrigine” OR “carbamazepine” OR “divalproex” OR “ziprasidone”)	178001
#6	Search (#4 or #5)	468727
#7	Search (#1 and #6)	1745
#8	Search (#3 or #7)	10088
#9	Search (#3 or #7) Filters: Humans	9314
#10	Search (#3 or #7) Filters: Humans; English	8614
#11	Search (#3 or #7) Filters: Humans; English; Adult: 19+ years	5091
#12	Search (#11 NOT (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt]))	4950
#13	Search (((randomized[title/abstract] OR randomised[title/abstract]) AND controlled[title/abstract] AND trial[title/abstract]) OR (controlled[title/abstract] AND trial[title/abstract]) OR "controlled clinical trial"[publication type] OR "Randomized Controlled Trial"[Publication Type] OR "Single-Blind Method"[MeSH] OR "Double-Blind Method"[MeSH] OR "Random Allocation"[MeSH]))	685802
#14	Search (#12 and #13)	918
#15	Search ("Comparative Study"[Publication Type] OR "comparative study" OR "case control study"[all fields] OR "case control studies"[all fields] OR "Case-Control Studies"[Mesh] OR "Cohort Studies"[Mesh] OR “cohort effect”[MeSH Term] OR cohort*[tiab] OR “prospective studies”[MeSH] OR ((prospective*[All Fields] AND cohort[All Fields] AND (study[All Fields] OR studies[All Fields])))	3525221
#16	Search (#12 and #15)	1533

Search	Query	Items found
#17	Search (#14 or #16)	2088
#18	Search (#14 or #16) Filters: Publication date from 2016/10/01 to 2017/12/31	76
#19	Search (("review"[Publication Type] AND "systematic"[tiab]) OR "systematic review"[All Fields] OR ("review literature as topic"[MeSH AND "systematic"[tiab]) OR "meta-analysis"[Publication Type] OR "meta-analysis as topic"[MeSH Terms] OR "meta-analysis"[All Fields])	215382
#20	Search (#12 and #19)	72
#21	Search (#12 and #19) Filters: Publication date from 2012/01/01 to 2017/12/31	5
#22	Search (“energy psychology”[All Fields] OR EFT OR “emotional freedom technique”[All Fields] OR "Monoamine Oxidase Inhibitors"[Mesh] OR "Naltrexone"[Mesh] OR "Cycloserine"[Mesh] OR "Adrenergic alpha-Antagonists"[Mesh] OR “Alpha blocker”[All Fields] OR “Alpha blockers”[All Fields] OR Olanzapine OR Risperidone OR Ziprazidone OR “mood stabilizer” [All Fields] OR “mood stabilizers” [All Fields] OR "Antidepressive Agents, Second-Generation"[Mesh] OR “second-generation antidepressants”[All Fields] OR “atypical antipsychotics” OR "Aripiprazole"[Mesh] OR Aripiprazole OR "Quetiapine Fumarate"[Mesh] OR Quetiapine)	67597
#23	Search (#1 and #22)	544
#24	Search (#1 and #22) Filters: Humans	457
#25	Search (#1 and #22) Filters: Humans; English	440
#26	Search (#1 and #22) Filters: Humans; English; Adult: 19+ years	257
#27	Search (#26 NOT (letter[pt] OR newspaper article[pt] OR editorial[pt] OR comment[pt]))	225
#28	Search (#27 and (#13 or #15)) Publication date from 2016/10/01 to 2017/12/31	11
#29	Search (#27 and #19) Publication date from 2016/10/01 to 2017/12/31	1

9/29/17 Cochrane Library

ID	Search	Hits
#1	[mh "Stress Disorders, Post-Traumatic"] or "post-traumatic stress disorder" or "post-traumatic stress disorders" or "posttraumatic stress disorder" or "posttraumatic stress disorders" or (disorder* and "post-traumatic") or [mh ^"Stress Disorders, Traumatic"] or [mh "Combat Disorders"] or PTSD or "stress disorder" or "traumatic event" or "traumatic incident"	3708
#2	[mh "implosive therapy"] or "implosive therapy" or (exposure and (therapy or psychotherapy)) or "imaginal exposure" or [mh "Biofeedback, Psychology"] or biofeedback or neurofeedback or [mh "Relaxation Therapy"] or "relaxation training" or [mh "cognitive therapy"] or cognitive restructur* or cognitive processing therap* or [mh "Adaptation, Psychological"] or coping skill* or "stress inoculation" or "assertiveness training" or (psychodynamic and ([mh /TH] or therapy or [mh therapeutics] or therapeutics)) or (psychodynamic and ([mh psychotherapy] or psychotherapy)) or (psychoanalytic and psychotherapy) or "psychoanalytic psychotherapy" or ("psycho-analytic" and psychotherapy) or "psycho-analytic psychotherapy" or "psychoanalytic therapy" or (psychoanalytic and therapy) or (psycho-analytic and therapy) or [mh "Eye Movement Desensitization Reprocessing"] or EMDR or [mh Psychotherapy] or "brief eclectic psychotherapy" or "interpersonal therapy" or "interpersonal psychotherapy" or "family therapy" or "marital therapy" or "group therapy" or "group psychotherapy" or "group psychological therapy" or [mh Hypnosis] or hypnotherapy or "eclectic psychotherapy"	45623
#3	#1 and #2	1607
#4	[mh Benzodiazepines] or [mh "Antidepressive Agents, Tricyclic"] or "tricyclic antidepressants" or [mh Anticonvulsants] or anticonvulsants or [mh "Adrenergic alpha-Antagonists"] or "adrenergic alpha-antagonists" or "Antipsychotic Agents" or antipsychotics or "Antidepressive Agents"	22788
#5	[mh "Serotonin Uptake Inhibitors"] or "Serotonin Uptake Inhibitors" or [mh "Serotonin and Noradrenaline Reuptake Inhibitors"] or SSRI or SSRIs or SNRI or SNRIs or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or desvenlafaxine or venlafaxine or duloxetine or imipramine or amitriptyline or desipramine or bupropion or mirtazapine or nefazodone or trazodone or prazosin or olanzapine or risperidone or [mh Benzodiazepines] or alprazolam or diazepam or lorazepam or clonazepam or topiramate or tiagabine or lamotrigine or carbamazepine or divalproex or ziprasidone	35897
#6	#4 or #5	43104
#7	#1 and #6	598
#8	#3 or #7	1999
#9	Adult*:ti,ab,kw or [mh Adult]	470877
#10	#8 and #9	1202
#11	#10 not (letter:pt or newspaper article:pt or editorial:pt or comment:pt) Publication Year from 2012 to 2017	52
#12	"energy psychology" or EFT or "emotional freedom technique" or [mh "Monoamine Oxidase Inhibitors"] or [mh Naltrexone] or [mh Cycloserine] or [mh "Adrenergic alpha-Antagonists"] or "Alpha blocker" or "Alpha blockers" or Olanzapine or Risperidone or Ziprazidone or "mood stabilizer" or "mood stabilizers" or [mh "Antidepressive Agents, Second-Generation"] or "second-generation antidepressants" or "atypical antipsychotics" or [mh Aripiprazole] or Aripiprazole or [mh "Quetiapine Fumarate"] or Quetiapine	10890
#13	#1 and #12	193
#14	#13 and #9	118
#15	#14 not #11	20

9/29/17 CINAHL (Cumulative Index to Nursing and Allied Health)

#	Query	Limiters/Expanders	Last Run Via	Results
S1	(MH "Stress Disorders, Post-Traumatic") or "post-traumatic stress disorder" or "post-traumatic stress disorders" or "posttraumatic stress disorder" or "posttraumatic stress disorders" or (disorder* and "post-traumatic") OR "Combat Disorders" or PTSD or "stress disorder" or "traumatic event" or "traumatic incident"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	19465
S2	"implosive therapy" or (exposure and (therapy or psychotherapy)) or "imaginal exposure" or biofeedback or neurofeedback or "Relaxation Therapy" or "relaxation training" or "cognitive therapy" or cognitive restructur* or cognitive processing therap* or "Adaptation, Psychological" OR “psychological adaptation” or coping skill* or "stress inoculation" or "assertiveness training" or (psychodynamic and (therapy or therapeutics)) or (psychodynamic and psychotherapy) or (psychoanalytic and psychotherapy) or "psychoanalytic psychotherapy" or ("psycho-analytic" and psychotherapy) or "psycho-analytic psychotherapy" or "psychoanalytic therapy" or (psychoanalytic and therapy) or (psycho-analytic and therapy) or "Eye Movement Desensitization Reprocessing" or EMDR or Psychotherapy or "brief eclectic psychotherapy" or "interpersonal therapy" or "interpersonal psychotherapy" or "family therapy" or "marital therapy" or "group therapy" or "group psychotherapy" or "group psychological therapy" or Hypnosis or hypnotherapy or "eclectic psychotherapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	88267
S3	S1 AND S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	3602
S4	(MH "Antianxiety Agents, Benzodiazepine") or (MH "Antidepressive Agents, Tricyclic") or "tricyclic antidepressants" or anticonvulsants or (MH "Adrenergic alpha-Antagonists") or "adrenergic alpha-antagonists" or "Antipsychotic Agents" or antipsychotics or "Antidepressive Agents"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	35845
S5	(MH "Serotonin Uptake Inhibitors") or "Serotonin Uptake Inhibitors" or "Noradrenaline Reuptake Inhibitors" or SSRI or SSRIs or SNRI or SNRIs or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or desvenlafaxine or venlafaxine or duloxetine or imipramine or amitriptyline or desipramine or bupropion or mirtazapine or nefazodone or trazodone or prazosin or olanzapine or risperidone or alprazolam or diazepam or lorazepam or clonazepam or topiramate or tiagabine or lamotrigine or carbamazepine or divalproex OR ziprasidone	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	23126

#	Query	Limiters/Expanders	Last Run Via	Results
S6	S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	50319
S7	S1 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	603
S8	S3 OR S7	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	4018
S9	S8	Limiters - Published Date: 20161001-20171231; English Language; Exclude MEDLINE records; Human; Language: English Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	95
S10	S9	Limiters - Publication Type: Clinical Trial, Randomized Controlled Trial Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	**0**
S11	S9	Limiters - Publication Type: Meta Analysis, Systematic Review Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	**0**
S12	"comparative study" OR (MH “comparative studies”) OR "case control study" OR (MH "case control studies") OR “Cohort Study” OR "Cohort Studies" OR “cohort effect” OR cohort* OR (MH “prospective studies”) OR ((prospective* AND cohort AND (study OR studies))	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	533512
S13	S9 AND S12	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	**18**

#	Query	Limiters/Expanders	Last Run Via	Results
S14	"energy psychology" or EFT or "emotional freedom technique" or (MH "Monoamine Oxidase Inhibitors") or Naltrexone or Cycloserine or "Alpha blocker" or "Alpha blockers" or Olanzapine or Risperidone or Ziprazidone or "mood stabilizer" or "mood stabilizers" or (MH "Antidepressive Agents, Second-Generation") or "second-generation antidepressants" or "atypical antipsychotics" or Aripiprazole or Quetiapine	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	9478
S15	S1 AND S14	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	130
S16	S15 NOT (S10 OR S11 OR S13)	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	128
S17	S16	Limiters - Published Date: 20161001-20171231 English Language; Exclude MEDLINE records; Human; Age Groups: All Adult: Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - CINAHL Plus with Full Text	**1**

9/29/17 PsycINFO

#	Query	Limiters/Expanders	Last Run Via	Results
S1	(DE "Post-Traumatic Stress") OR "post-traumatic stress disorder" OR "post-traumatic stress disorders" OR “posttraumatic stress disorder” OR “posttraumatic stress disorders” OR (disorder* AND "post-traumatic") OR “Combat Disorder” OR "Combat Disorders” OR PTSD OR "stress disorder" OR "traumatic event" OR "traumatic incident"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	46770
S2	(DE "implosive therapy") OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR “imaginal exposure” OR (DE “Biofeedback, Psychiatry”) OR biofeedback or neurofeedback OR (DE “Relaxation Therapy”) OR “relaxation training” OR (DE “cognitive therapy”) OR cognitive restructur* OR “cognitive processing therapy” OR “Psychological Adaptation” OR coping skill* OR "stress inoculation" OR “assertiveness training” OR (DE “Psychodynamic Psychotherapy) OR (psychodynamic AND ("therapy" OR "therapeutics")) OR (psychodynamic AND "psychotherapy") OR ("psychoanalytic" AND "psychotherapy") OR "psychoanalytic psychotherapy" OR ("psycho-analytic" AND "psychotherapy”) OR "psycho-analytic psychotherapy" OR "psychoanalytic therapy" OR "psycho-analytic therapy" OR (DE “Eye Movement Desensitization Therapy”) OR “eye movement desensitization reprocessing” OR EMDR OR (DE "Psychotherapy") OR “brief eclectic psychotherapy” OR "interpersonal therapy” OR “interpersonal psychotherapy” OR "family therapy" OR "marital therapy" OR “group therapy” OR “group psychotherapy” OR “group psychological therapy” OR Hypnosis OR hypnotherapy OR "eclectic psychotherapy"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	57261
S3	S1 AND S2	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	4149
S4	(DE "Benzodiazepines") OR (DE “Antidepressant Drugs”) OR "Tricyclic Antidepressive Agents" OR (DE Tricyclic Antidepressant Drugs”) OR (DE “Anticonvulsive Drugs”) OR Anticonvulsants OR "Adrenergic alpha-Antagonists" OR (DE “Neuroleptic Drugs”) OR "Antipsychotic Agents"	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	26648

#	Query	Limiters/Expanders	Last Run Via	Results
S5	"Serotonin Uptake Inhibitors" OR (DE "Serotonin and Norepinephrine Reuptake Inhibitors") OR SSRI* OR SNRI* OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines [MeSH] OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	54055
S6	S4 OR S5	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	67650
S7	S1 AND S6	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	1157
S8	S7	Limiters - Publication Year: 2016-2017; English; Age Groups: Adulthood (18 yrs & older); Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	44
S9	S8	Limiters - Methodology: CLINICAL CASE STUDY, CLINICAL TRIAL, EMPIRICAL STUDY, -Experimental Replication, -Followup Study, -Longitudinal Study, ---Prospective Study, ---Retrospective Study, QUALITATIVE STUDY, QUANTITATIVE STUDY, TREATMENT OUTCOME Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	40
S10	S8	Limiters - Methodology: -Systematic Review, META ANALYSIS Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	2

#	Query	Limiters/Expanders	Last Run Via	Results
S11	“energy psychology” OR EFT OR “emotional freedom technique” OR (DE "Monoamine Oxidase Inhibitors”) OR Naltrexone OR Cycloserine OR "Adrenergic alpha-Antagonists" OR “alpha blocker” OR “alpha blockers” OR Olanzapine OR Risperidone OR Ziprazidone OR (DE “Mood Stabilizers”) OR “mood stabilizer” OR “mood stabilizers” OR “second-generation antidepressants”[All Fields] OR “atypical antipsychotics” OR Aripiprazole OR Quetiapine	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	26051
S12	S1 AND S11	Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	421
S13	S12	Limiters - Publication Year: 2016-2017; English; Language: English; Age Groups: Adulthood (18 yrs & older); Population Group: Human Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	22
S14	S13	Limiters - Methodology: CLINICAL CASE STUDY, CLINICAL TRIAL, EMPIRICAL STUDY, -Experimental Replication, -Followup Study, -Longitudinal Study, --- Prospective Study, --- Retrospective Study, QUALITATIVE STUDY, QUANTITATIVE STUDY, TREATMENT OUTCOME Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	20
S15	S12	Limiters - Methodology: -Systematic Review, META ANALYSIS Search modes - Boolean/Phrase	Interface - EBSCOhost Research Databases Search Screen - Advanced Search Database - PsycINFO	11

9/29/17 Published International Literature on Traumatic Stress (PILOTS)

Set#	Searched for	Databases	Results
S1	("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	37202
S2	SU.EXACT("Adults") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	23320
S3	(("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	16773
S4	("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	11832

Set#	Searched for	Databases	Results
S5	((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	3608
S6	("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone) AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	1413

Set#	Searched for	Databases	Results
S7	((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone) AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	538

Set#	Searched for	Databases	Results
S8	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone) AND la.exact("English")))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	4051
S9	("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	5791

Set#	Searched for	Databases	Results
S10	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone) AND la.exact("English")))) AND (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	1279

Set#	Searched for	Databases	Results
S11	("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English") AND pd(20161001-20171231)	PILOTS: Published International Literature On Traumatic Stress	414
S12	("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English") AND pd(20161001-20171231)	PILOTS: Published International Literature On Traumatic Stress	117

Set#	Searched for	Databases	Results
S13	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone) AND la.exact("English")))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English") AND pd(20161001-20171231))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	9

Set#	Searched for	Databases	Results
S15	("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	383
S16	((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	131
S17	("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	5791
S18	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	83

Set#	Searched for	Databases	Results
S19	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English"))) NOT (("randomized clinical trial" OR "single-blind" OR "double-blind" OR "random allocation" OR "comparative study" OR case control stud* OR "cohort studies" OR "cohort effect" OR cohort* OR trial OR "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR "prospective studies") AND la.exact("English") AND pd(20161001-20171231))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	77
S20	("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English")	PILOTS: Published International Literature On Traumatic Stress	1249
S21	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English"))	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	6

S22	(((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR "Naltrexone" OR " Cycloserine " OR " Adrenergic alpha-Antagonists " OR "Alpha blocker" OR "Alpha blockers" OR Olanzapine OR Risperidone OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR " Antidepressive Agents, Second-Generation" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine) AND la.exact("English"))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English"))) NOT ((((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy") AND la.exact("English"))) OR ((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND la.exact("English")) AND (SU.EXACT("Adults") AND la.exact("English"))) AND (("benzodiazepine derivatives" OR "tricyclic derivatives" OR "antimanic drugs" OR anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" OR "antiadrenergic agents" OR "antipsychotic drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR "antidepressant drugs" OR "antiadrenergic agents" OR citalopram OR escitalopram OR fluoxetine OR	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	6

Set#	Searched for	Databases	Results
	fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone) AND la.exact("English")))) AND (("meta analysis" OR "meta-analysis" OR "systematic review" OR (review AND systematic) OR ("review literature as topic" AND systematic)) AND la.exact("English") AND pd(20161001-20171231)))		

Set#	Searched for	Databases	Results
S23	((((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND SU.EXACT("Adults")) AND ("exposure therapy" OR "implosive therapy" OR (exposure AND (therapy OR psychotherapy)) OR "imaginal exposure" OR "cognitive therapy" OR cognitive restructur* OR cognitive processing therap* OR "psychological adaptation" OR "coping behavior" OR coping skill* OR "stress inoculation" OR "assertiveness training" OR (psychodynamic AND ("psychotherapy" OR psychotherapy)) OR (psychodynamic AND (therapy OR therapeutics)) OR (psychoanalytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR (psycho-analytic AND (psychotherapy OR "psychoanalytic psychotherapy")) OR "psychoanalytic therapy" OR "psychotherapy" OR "interpersonal therapy" OR "interpersonal psychotherapy" OR "Eye Movement Desensitization Reprocessing" OR EMDR OR "family therapy" OR "marital therapy" OR "group therapy" OR "group psychotherapy" OR "group psychological therapy" OR "hypnotherapy" OR "imaginal exposure" OR biofeedback OR neurofeedback OR "relaxation therapy" OR "relaxation training" OR "eclectic psychotherapy")) OR ((("PTSD " OR (" post-traumatic stress disorder " OR " post-traumatic stress disorders ") OR (disorder* AND " post-traumatic ") OR (" combat disorders ") OR "posttraumatic stress disorder" OR "posttraumatic stress disorders" OR " stress disorder " OR " traumatic event " OR " traumatic incident") AND SU.EXACT("Adults")) AND ("benzodiazepine derivatives" or "tricyclic derivatives" or "antimanic drugs" or anticonvulsant* OR "anticonvulsant drug" OR "anticonvulsant drugs" or “antiadrenergic agents" or “antipsychotic drugs" or "antiadrenergic agents" or “antidepressant drugs" or "antiadrenergic agents" or “antidepressant drugs" or "antiadrenergic agents" or citalopram OR escitalopram OR fluoxetine OR fluvoxamine OR paroxetine OR sertraline OR desvenlafaxine OR venlafaxine OR duloxetine OR imipramine OR amitriptyline OR desipramine OR bupropion OR mirtazapine OR nefazodone OR trazodone OR prazosin OR olanzapine OR risperidone OR benzodiazepines OR alprazolam OR diazepam OR lorazepam OR clonazepam OR topiramate OR tiagabine OR lamotrigine OR carbamazepine OR divalproex OR ziprasidone))) AND ("randomized clinical trial" or "single-blind" or "double-blind" or "random allocation" or "comparative study" OR case control stud* or "cohort studies" OR "cohort effect" OR cohort* or trial or "treatment outcome" OR "treatment outcomes" OR (prospective* AND cohort*) OR “ prospective studies”) AND pd(20161001-20171231)	PILOTS: Published International Literature On Traumatic Stress These databases are searched for part of your query.	144

Gray Literature Search for Trials in ClinicalTrials.gov, 10-2-17 **– 622** records total.
Main search (**155** results, all imported):

EXACT Completed [OVERALL-STATUS] AND NOT NOTEXT [RESULTS-FIRST-SUBMITTED] AND (posttraumatic and disorder*) OR (disorder* and AND "post-traumatic") or "Combat Disorders" OR PTSD OR ("stress disorder" AND (traumatic AND (event or incident))) [DISEASE] AND “implosive therapy AND "or (exposure and (therapy or psychotherapy)) or" AND imaginal exposure AND "or biofeedback or neurofeedback or" AND Relaxation Therapy AND "or" AND relaxation training AND "or “cognitive therapy" AND or cognitive restructur* or cognitive processing therap* or “psychological adaptation” or coping skill* or AND "stress inoculation" AND or AND "assertiveness training" AND or AND psychodynamic and AND therapy or therapeutics AND or AND psychodynamic and psychotherapy AND or AND psychoanalytic and psychotherapy AND or AND "psycho-analytic" AND and psychotherapy AND or AND psychoanalytic and therapy AND or AND psycho-analytic and therapy AND or AND "Eye Movement Desensitization Reprocessing" AND or EMDR or Psychotherapy or AND "interpersonal therapy" AND or AND "interpersonal psychotherapy" AND or AND "family therapy" AND or AND "marital therapy" AND or AND "group therapy" AND or AND "group psychotherapy" AND or AND "group psychological therapy" AND or Hypnosis or hypnotherapy or AND "eclectic psychotherapy" OR Benzodiazepines or AND "Antidepressive Agents” or" AND tricyclic antidepressants AND "or Anticonvulsants or" AND Adrenergic alpha-Antagonists AND "or" AND Antipsychotic Agents AND "or antipsychotics or “Serotonin Uptake Inhibitors" AND or AND "Serotonin and Noradrenaline Reuptake Inhibitors" AND or SSRI or SSRIs or SNRI or SNRIs or citalopram or escitalopram or fluoxetine or fluvoxamine or paroxetine or sertraline or desvenlafaxine or venlafaxine or duloxetine or imipramine or amitriptyline or desipramine or bupropion or mirtazapine or nefazodone or trazodone or prazosin or alprazolam or diazepam or lorazepam or clonazepam or topiramate or tiagabine or lamotrigine or carbamazepine or divalproex or ziprasidone [TREATMENT] AND EXACT (Adult OR Senior) [AGE-GROUP] | Completed Studies | Studies With Results

New interventions search (626 results, **467** imported):

(EXACT Completed [OVERALL-STATUS] AND NOT NOTEXT [RESULTS-FIRST-SUBMITTED] AND posttraumatic and disorder* OR disorder* and AND "post-traumatic" AND or AND "Combat Disorders" OR PTSD OR ("stress disorder" AND traumatic AND event or incident) [DISEASE] AND "energy psychology" OR EFT OR "emotional freedom technique" OR "Monoamine Oxidase Inhibitors" OR Naltrexone OR Cycloserine OR "Adrenergic alpha-Antagonists" OR "Alpha blocker" OR "Alpha blockers" OR Ziprazidone OR "mood stabilizer" OR "mood stabilizers" OR "second-generation antidepressants" OR "atypical antipsychotics" OR Aripiprazole OR Quetiapine [TREATMENT] AND EXACT (Adult OR Senior) [AGE-GROUP]) AND EXACT Completed [OVERALL-STATUS] AND NOT NOTEXT [RESULTS-FIRST-SUBMITTED]

Appendix D. Excluded Studies

X1: Not original research
X2: Ineligible study design
X3: Ineligible population
X4: Ineligible intervention
X5: Ineligible comparator
X6: Ineligible outcome
X7: Ineligible study duration
X8: Ineligible setting
X9: Ineligible sample size
X10: Not in English
X11: Irretrievable
X12: Retracted

1. Psychotherapies for panic disorder: A tale of two sites. Journal of Clinical Psychiatry. 77 (7) (pp 927-935), 2016. Date of Publication: July 2016.; 2016. Exclusion Code: X3.
2. Acierno RE, Gros DF, Ruggiero KJ, et al. Behavioral activation and therapeutic exposure for posttraumatic stress disorder: a noninferiority trial of treatment delivered in person versus home-based telehealth. Depress Anxiety. 2016-12-01;33(5):415-23. doi: http://dx.doi.org/10.1002/da.22476. PMID: 1844925103; 45795. Exclusion Code: X5.
3. Acierno RE, Knapp RG, Tuerk PW, et al. A non-inferiority trial of prolonged exposure for posttraumatic stress disorder: in person versus home-based telehealth. Behav Res Ther. 2016-12-29;89:57-65. doi: http://dx.doi.org/10.1016/j.brat.2016.11.009. PMID: 1853730980; 45948. Exclusion Code: X5.
4. Aderka IM, Gillihan SJ, McLean CP, et al. The relationship between posttraumatic and depressive symptoms during prolonged exposure with and without cognitive restructuring for the treatment of posttraumatic stress disorder. J Consult Clin Psychol. 2013 Jun;81(3):375-82. doi: 10.1037/a0031523. PMID: 23339538. Exclusion Code: X5.
5. Ahearn EP, Krohn A, Connor KM, et al. Pharmacologic treatment of posttraumatic stress disorder: a focus on antipsychotic use. Ann Clin Psychiatry. 2016-09-15;15(3/4):193-201. doi: http://dx.doi.org/10.1023/B:ACLI.0000008173.01153.4e. PMID: 42422469; 26213. Exclusion Code: X2.
6. Ahmadi K, Hazrati M, Ahmadizadeh M, et al. REM desensitization as a new therapeutic method for post-traumatic stress disorder: a randomized controlled trial. Acta Med Indones. 2015 Apr;47(2):111-9. PMID: 26260553. Exclusion Code: X3.
7. Ahmadi N, Moss L, Simon E, et al. Efficacy and long-term clinical outcome of comorbid posttraumatic stress disorder and major depressive disorder after electroconvulsive therapy. Depress Anxiety. 2017-01-16;33(7):640-7. doi: http://dx.doi.org/10.1002/da.22451. PMID: 1758136749; 44580. Exclusion Code: X4.
8. Ahmadpanah M, Sabzeiee P, Hosseini SM, et al. Comparing the effect of prazosin and hydroxyzine on sleep quality in patients suffering from posttraumatic stress disorder. Neuropsychobiology. 2014;69(4):235-42. doi: 10.1159/000362243. PMID: 24993832. Exclusion Code: X5.
9. Albert U, Carmassi C, Cosci F, et al. Role and clinical implications of atypical antipsychotics in anxiety disorders, obsessive-compulsive disorder, trauma-related, and somatic symptom disorders: A systematized review. Int Clin Psychopharmacol. 2016;31(5):249-58. doi: 10.1097/YIC.0000000000000127. PMID: 2016-40188-002. Exclusion Code: X2.

10. Aldahadha B, Al-Harthy H, Sulaiman S. The Efficacy of Eye Movement Desensitization Reprocessing in Resolving the Trauma Caused by the Road Accidents in the Sultanate of Oman. Journal of Instructional Psychology. 2012;39(3/4):146-58. PMID: 107974814. Language: English. Entry Date: 20131007. Revision Date: 20150712. Publication Type: Journal Article. Exclusion Code: X3.

11. Alghamdi M, Hunt N, Thomas S. The effectiveness of Narrative Exposure Therapy with traumatised firefighters in Saudi Arabia: a randomized controlled study. Behav Res Ther. 2015 Mar;66:64-71. doi: 10.1016/j.brat.2015.01.008. PMID: 25701801. Exclusion Code: X3.

12. Allan NP, Short NA, Albanese BJ, et al. Direct and Mediating Effects of an Anxiety Sensitivity Intervention on Posttraumatic Stress Disorder Symptoms in Trauma-Exposed Individuals. Cogn Behav Ther. 2015;44(6):512-24. doi: 10.1080/16506073.2015.1075227. PMID: 26427912. Exclusion Code: X6.

13. Allen AR, Newby JM, Smith JC, et al. Internet-based cognitive behavioural therapy (iCBT) for posttraumatic stress disorder versus waitlist control: study protocol for a randomised controlled trial. Trials. 2016-09-28;16(1)doi: http://dx.doi.org/10.1186/s13063-015-1059-5. PMID: 1823905154; 45339. Exclusion Code: X6.

14. Amos T, Stein DJ, Ipser JC. Pharmacological interventions for preventing post-traumatic stress disorder (PTSD). Cochrane Database Syst Rev. 2014 Jul 08(7):Cd006239. doi: 10.1002/14651858.CD006239.pub2. PMID: 25001071. Exclusion Code: X3.

15. Andersen TE, Lahav Y, Ellegaard H, et al. A randomized controlled trial of brief somatic experiencing for chronic low back pain and comorbid post-traumatic stress disorder symptoms. European Journal of Psychotraumatology. 2017 2017-07-06;8(1)doi: http://dx.doi.org/10.1080/20008198.2017.1331108. PMID: 1916303335; 48054. Exclusion Code: X3.

16. Anderson ML, Najavits LM. Does seeking safety reduce PTSD symptoms in women receiving physical disability compensation? Rehabil Psychol. 2014 Aug;59(3):349-53. doi: 10.1037/a0036869. PMID: 24978844. Exclusion Code: X3.

17. Arnone R, Orrico A, D'Aquino G, et al. [EMDR and psychopharmacological therapy in the treatment of the post-traumatic stress disorder]. Rivista di psichiatria; 2012. p. 8-11. Exclusion Code: X10.

18. Baas MAM, Stramrood CAI, Dijksman LM, et al. The OptiMUM-study: EMDR therapy in pregnant women with posttraumatic stress disorder after previous childbirth and pregnant women with fear of childbirth: design of a multicentre randomized controlled trial. European Journal of Psychotraumatology. 2017-03-30;8(1)doi: http://dx.doi.org/10.1080/20008198.2017.1293315. PMID: 1882073329; 47084. Exclusion Code: X6.

19. Baker DG, Diamond BI, Gillette G, et al. A double-blind, randomized, placebo-controlled, multi-center study of brofaromine in the treatment of post-traumatic stress disorder. Psychopharmacology (Berl). 1995 Dec;122(4):386-9. PMID: 8657838. Exclusion Code: X4.

20. Baniasadi M, Hosseini G, Fayyazi Bordbar MR, et al. Effect of pregabalin augmentation in treatment of patients with combat-related chronic posttraumatic stress disorder: a randomized controlled trial. J Psychiatr Pract. 2014 Nov;20(6):419-27. doi: 10.1097/01.pra.0000456590.12998.41. PMID: 25406046. Exclusion Code: X4.

21. Barrera TL, Mott JM, Hofstein RF, et al. A meta-analytic review of exposure in group cognitive behavioral therapy for posttraumatic stress disorder. Clin Psychol Rev. 2016-09-15;33(1):24-32. doi: http://dx.doi.org/10.1016/j.cpr.2012.09.005. PMID: 1284061343; 39700. Exclusion Code: X2.

22. Bass JK, Annan J, McIvor Murray S, et al. Controlled trial of psychotherapy for Congolese survivors of sexual violence. N Engl J Med. 2013 Jun 06;368(23):2182-91. doi: 10.1056/NEJMoa1211853. PMID: 23738545. Exclusion Code: X3.

23. Belsher BE, Jaycox LH, Freed MC, et al. Mental health utilization patterns during a stepped, collaborative care effectiveness trial for PTSD and depression in the military health system. Med Care. 2016-09-15;54(7)doi: http://dx.doi.org/10.1097/MLR.0000000000000545. PMID: 1812432301; 45093. Exclusion Code: X4.

24. Bergen-Cico D, Possemato K, Pigeon W. Reductions in cortisol associated with primary care brief mindfulness program for veterans with PTSD. Med Care. 2014 Dec;52(12 Suppl 5):S25-31. doi: 10.1097/mlr.0000000000000224. PMID: 25397819. Exclusion Code: X4.

25. Berger R, Abu-Raiya H, Benatov J. Reducing primary and secondary traumatic stress symptoms among educators by training them to deliver a resiliency program (ERASE-Stress) following the Christchurch earthquake in New Zealand. Am J Orthopsychiatry. 2016 Mar;86(2):236-51. doi: 10.1037/ort0000153. PMID: 26963188. Exclusion Code: X3.

26. Berger W, Mendlowicz MV, Marques-Portella C, et al. Pharmacologic alternatives to antidepressants in posttraumatic stress disorder: A systematic review. Prog Neuropsychopharmacol Biol Psychiatry. 2009;33(2):169-80. doi: 10.1016/j.pnpbp.2008.12.004. PMID: 2009-02892-001. Exclusion Code: X2.

27. Bisson JI, Roberts NP, Andrew M, et al. Psychological therapies for chronic post-traumatic stress disorder (PTSD) in adults. Cochrane Database Syst Rev. 2013 Dec 13(12):Cd003388. doi: 10.1002/14651858.CD003388.pub4. PMID: 24338345. Exclusion Code: X2.

28. Bolton P, Bass JK, Zangana GA, et al. A randomized controlled trial of mental health interventions for survivors of systematic violence in Kurdistan, Northern Iraq. BMC Psychiatry. 2014 Dec 31;14:360. doi: 10.1186/s12888-014-0360-2. PMID: 25551436. Exclusion Code: X3.

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Appendix E. Risk of Bias Assessment

Table E-1. Risk of bias assessments, part 1

Author, Year	Was randomi-zation adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Acarturk, 2016[44]	Yes	Yes	Unclear	Yes	No	No	Overall: 71.4 G1: 67.3 G2: 75.5	Yes	No
Acosta, 2017[149]	Unclear	Unclear	Yes	Unclear	No	No	Overall: 76.5 G1: 81.5 G2: 71.6	Yes	No
Ahmadizadeh, 2013[198]	Unclear	Unclear	Unclear	Unclear	No	No	Unclear	NR	NR
Akuchekian et al., 2004[77]	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	93 94 91	No	No
Arntz et al., 2007[199]	Unclear	Unclear	Yes	Unclear	No	No	45 72	Yes	Yes
Asukai et al., 2010 [10]	Yes	Unclear	Yes	Yes	No	No	75 92	No	Yes
Bartzokis et al., 2005[86]	Unclear	Unclear	Unclear	Yes	Yes	Yes	74 67 81	Yes	No
Basoglu et al., 2007[11]	Yes	Yes	Yes	No	No	No	100 100 100	No	No
Batki et al., 2014[165]	Yes	Yes	Yes	Yes	Yes	Yes	Overall: 90 G1: 87.5 G2: 92.9	No	No
Beck et al., 2009[200]	Unclear	Unclear	Unclear	Unclear	No	No	75 65 89	Yes	Yes
Becker et al., 2007[183]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	90 to 100 83 to 100	No	No
Beidel et al., 2011[201]	Unclear	Unclear	Unclear	Unclear	No	No	86 78 94	No	Yes

Author, Year	Was randomi-zation adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Bichescu et al., 2007[202]	Unclear	Unclear	Yes	No	No	No	100 100 100	No	No
Blanchard et al., 2003[36]	Unclear	Unclear	Yes	Yes	No	No	80 73 75 96	Yes	Yes
Boden et al., 2012[58]	Yes	Unclear	No	Yes	No	No	84 83 85	Yes	No
Bohus et al., 2013[23]	Unclear	Unclear	Yes	Yes	No	No	Overall: 73 G1: 82 G2: 65	Yes	Yes
Brady et al., 2000[66]	Unclear	Unclear	No	Unclear	Unclear	Yes	69 68 70	Yes	No

Table E-2. Risk of bias assessments, part 2

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Acarturk, 2016[44]	Yes	LOCF	Yes	Yes	NA	Med
Acosta, 2017[149]	Yes	CA	Yes	Yes	No	Med
Ahmadizadeh, 2013[198]	No	Unclear	Yes	Yes	No	High
Akuchekian et al., 2004[77]	No	CA	Yes	Not Assessed	NA	Med
Arntz et al., 2007[199]	Yes	LOCF	Yes	Not Assessed	No	High
Asukai et al., 2010 [10]	Yes	MI	Yes	Not Assessed	Mixed	Med
Bartzokis et al., 2005[86]	No	Other	Yes	Not Assessed	NA	Med
Basoglu et al., 2007[11]	No	NA	Yes	Not Assessed	No	Med
Batki et al., 2014[165]	Yes	Unclear	Yes	Yes	NA	Low
Beck et al., 2009[200]	No	CA	Yes	Not Assessed	Yes	High
Becker et al., 2007[183]	Yes	LOCF	Yes	Not Assessed	NA	Med
Beidel et al., 2011[201]	No	CA	Yes	Not Assessed	Yes	High
Bichescu et al., 2007[202]	NA	NA	Yes	Not Assessed	No	High
Blanchard et al., 2003[36]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Boden et al., 2012[58]	Yes	Unclear	Yes	Not Assessed	Yes	Med
Bohus et al., 2013[23]	Yes	Mixed	Yes	Yes	No	Med
Brady et al., 2000[66]	Yes	LOCF	Yes	Not Assessed	NA	Med

Table E-3. Risk of bias assessments, part 3

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Brady et al., 2005[67]	Yes	Unclear	Yes	Unclear	Yes	Yes	63 69	Yes	No
Braun et al., 1990[169]	Unclear	Unclear	Unclear	Yes	Unclear	Yes	63 57 67	Yes	No
Brom et al., 1989[203]	Unclear	Unclear	Unclear	Unclear	No	No	89 90 90 90 87	No	No
Bryant, et al., 2003[41]	Unclear	Unclear	Yes	Yes	No	No	78 75 75 83	Yes	No
Bryant et al., 2008[42]	Yes	Yes	Yes	Yes	No	No	76 74 79 68 86	Yes	No
Butollo et al., 2016[204]	Unclear	Unclear	No	Unclear	No	No	Overall: 59.5 G1: 66.2 G2: 52.7	Yes	No
Butterfield et al., 2001[82]	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	73 70 80	Yes	No
Carey et al., 2012[81]	Yes	Yes	No	Unclear	Yes	Yes	Overall: 63.2	Yes	NR
Carlson et al., 1998[46]	Unclear	Unclear	No	No	No	No	97 92 100 100	No	No
Chard et al., 2005[2]	Unclear	Unclear	Yes	Yes	No	No	82 83 80	No	No

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Church et al., 2013[155]	Unclear	Yes	Yes	No	No	No	Overall: 92 G1: 97 G2: 86	No	No
Cloitre et al., 2002[37]	Unclear	Unclear	Unclear	Yes	No	No	79 71 89	Yes	Yes

Table E-4. Risk of bias assessments, part 4

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Brady et al., 2005[67]	Yes	Other	Yes	Not Assessed	NA	Med
Braun et al., 1990[169]	No	CA	No	Not Assessed	NA	High
Brom et al., 1989[203]	No	CA	Mixed	Not Assessed	No	High
Bryant, et al., 2003[41]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Bryant et al., 2008[42]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Butollo et al., 2016[204]	Yes	LOCF	Yes	Yes	NA	High
Butterfield et al., 2001[82]	Yes	CA	Yes	Not Assessed	NA	Med
Carey et al., 2012[81]	Yes	LOCF	Yes	Yes	NA	Med
Carlson et al., 1998[46]	No	Unclear	Yes	Not Assessed	No	Med (post-treatment) High (3- & 9-mth)
Chard et al., 2005[2]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Church et al., 2013[155]	No	CA	Yes	Yes	No	Med
Cloitre et al., 2002[37]	Yes	LOCF	Yes	Not Assessed	Yes	Med

Table E-5. Risk of bias assessments, part 5

Author, Year	Was randomi-zation adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Cloitre et al., 2010 [148] Cloitre et al., 2016[150]	Unclear	No	Yes	Yes	No	Unclear	73 85 74 61 3 Month 68 76 68 61 6 Month 63 70 61 61	Yes	Yes
Coffey, 2017[140]	Yes	Unclear	Yes	Yes	No	No	Overall: 77.8 G1: 87.8 G2: 62.2 G3: 60	Yes	Yes
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171]	Yes	Yes	No	Yes	Yes	Yes	67 78 59	Yes	Yes
Cook et al., 2010 [156]	Yes	Unclear	Yes	Yes	No	Unclear	73 81 64	Yes	Yes
Cottraux, 2008[31]	Yes	Yes	Yes	Yes	No	No	70 87 52	Yes	Yes
Davidson et al., 1990[179] Davidson et al., 1993[180]	Unclear	Unclear	Yes	Yes	Yes	Yes	72 68 76	Yes	No
Davidson et al., 2001[68]	Yes	Unclear	Yes	Unclear	Unclear	Yes	66 67 66	Yes	No

Table E-6. Risk of bias assessments, part 6

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Cloitre et al., 2010 [148] Cloitre et al., 2016[150]	Yes	MI	Yes	Not Assessed	Yes	Med
Coffey, 2017[140]	Yes	MI	Yes	Yes	Yes	Med
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171]	Yes	LOCF	Mixed	Not Assessed	NA	Med
Cook et al., 2010 [156]	Yes	MI	Yes	Not Assessed	Yes	Med
Cottraux, 2008[31]	Yes	LOCF	Yes	Not Assessed	No	Med
Davidson et al., 1990[179] Davidson, et al., 1993[180]	No	CA	Yes	Not Assessed	NA	High
Davidson et al., 2001[68]	Yes	Other	Yes	Not Assessed	NA	Med

Table E-7. Risk of bias assessments, part 7

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Davidson et al., 2003[184]	Unclear	Unclear	Yes	Unclear	Yes	Yes	82 67	Yes	Yes
Davidson et al., 2006[69]	Unclear	Unclear	Unclear	Unclear	Yes	Yes	65 NR NR	Yes	No
Davidson et al., 2006[73]	Yes	Unclear	Yes	Unclear	Yes	Yes	68 70 67	Yes	No
Davidson et al., 2007[166]	Unclear	Unclear	Unclear	Yes	Yes	Yes	61 66 55	Yes	No
Davis et al., 2004[205]	Unclear	Yes	No	Yes	Yes	Yes	55 52 60	Yes	No
Davis et al., 2008[164]	Yes	Yes	Yes	Yes	Yes	Yes	77 83	Yes	No
Difede et al., 2007[206]	Unclear	Yes	Yes	Yes	No	No	68 47 88	Yes	Yes
Dorrepaal et al., 2012[207]	Unclear	Yes	No	Unclear	No	No	Overall: 84.5 G1: 84.8 G2: 81.6	No	No
Dunne et al., 2012[208]	Unclear	Unclear	Yes	No	No	No	Overall: 88.5 G1: 84.6 G2: 92.3	No	No

Table E-8. Risk of bias assessments, part 8

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Davidson et al., 2003[184]	Yes	LOCF	Yes	Not Assessed	NA	Med
Davidson et al., 2006[69]	Yes	LOCF	Yes	Not Assessed	NA	Med
Davidson et al., 2006[73]	Yes	LOCF	Yes	Not Assessed	NA	Med
Davidson et al., 2007[166]	No	LOCF	Yes	Not Assessed	NA	Med
Davis et al., 2004[205]	Yes	LOCF	Yes	Not Assessed	NA	High
Davis et al., 2008[164]	Yes	LOCF	Yes	Not Assessed	NA	Low
Difede et al., 2007[206]	Yes	LOCF	Yes	Not Assessed	Yes	High
Dorrepaal et al., 2012[207]	Yes	Mixed	Yes	Yes	No	High
Dunne et al., 2012[208]	Yes	LOCF	Yes	Yes	No	High

Table E-9. Risk of bias assessments, part 9

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Ehlers et al., 2003[5]	Yes	Yes	Unclear	Yes	No	No	100 89 90	No	No
Ehlers et al., 2005[8]	Unclear	Unclear	Yes	Yes	No	No	100 100 100	No	No
Ehlers et al., 2014[9]	Unclear	Yes	Yes	Yes	No	No	G1: 100 G2: 96.7 G3: 96.8 G4: 90	No	No
Engel et al., 2015[26]	Unclear	Yes	Yes	Yes	Yes	No	Overall: 82.5 G1: 86.5 G2: 79.1	No	No
Fecteau et al., 1999[38]	Unclear	Unclear	No	No	No	No	83 91	No	No
Feske et al., 2008[209]	Unclear	Unclear	Yes	Unclear	No	No	78 69 86	Yes	Yes
Foa et al., 1991[210]	Unclear	Unclear	No	Yes	No	No	82 82 71 79 100	No	Yes
Foa et al., 2005[12]	No	Yes	No	Yes	No	No	64 66 59 96	Yes	Yes
Foa et al., 1999[14] Zoellner et al., 1999[134]	Unclear	Unclear	Unclear	Yes	No	No	82 92 73 73 100	No	Yes

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Fonzo et al., 2017[137] Fonzo et al., 2017[21]	Yes	Unclear	Yes	Unclear	No	No	Overall: 77 G1: 69 G2: 87	Yes	Yes
Forbes et al., 2012[4]	Yes	Yes	Yes	Yes	No	No	78 80 79	Yes	No
Ford et al., 2011[59]	Yes	Yes	Unclear	No	No	No	71 71 66 78	Yes	No
Ford et al., 2013[60]	Yes	Yes	Yes	Unclear	No	No	Overall:90 G1: 93 G2: 87	No	No
Franklin et al., 2017 [211]	Yes	Unclear	Unclear	Yes	No	No	Overall: 60 G1: 30 G2: 57 G3: 100	Yes	Yes
Friedman et al., 2007[70]	Yes	Unclear	Yes	Yes	Unclear	Yes	70 83	Yes	No

Table E-10. Risk of bias assessments, part 10

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Ehlers et al., 2003[5]	Yes	Unclear	Yes	Not Assessed	No	Med
Ehlers et al., 2005[8]	No	NA	Yes	Not Assessed	Mixed	Med
Ehlers et al., 2014[9]	Yes	LOCF	Yes	Yes	Yes	Low
Engel et al., 2015[26]	Yes	Other	Yes	Yes	NA	Med
Fecteau et al., 1999[38]	No	CA	Yes	Not Assessed	Yes	Med
Feske et al., 2008[209]	No	CA	Yes	Not Assessed	No	High
Foa et al., 1991[210]	No	CA	Yes	Not Assessed	No	High
Foa et al., 2005[12]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Foa et al., 1999[14] Zoellner et al., 1999[134]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Fonzo et al., 2017[137] Fonzo et al., 2017[21]	Yes	Unclear	Yes	Yes	Yes	Med
Forbes et al., 2012[4]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Ford et al., 2011[59]	Yes	Mixed model regression	Yes	Not Assessed	Yes	Med
Ford et al., 2013[60]	No	NA	Yes	Yes	Yes	Med
Franklin et al., 2017 [211]	No	CA	Yes	Yes	Yes	High
Friedman et al., 2007[70]	Yes	LOCF	Yes	Not Assessed	NA	Med

Table E-11. Risk of bias assessments, part 11

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Frommberger et al., 2004[212]	Unclear	Unclear	Unclear	Unclear	Unclear	No	76 80 73	Yes	No
Galovski et al., 2012[6]	Yes	Yes	Yes	Yes	No	No	Overall: 70 G1: 78.7 G2: 62.3	Yes	Yes
Galovski et al., 2016[213]	Yes	Yes	Yes	Yes	Unclear	Unclear	Overall: 55.4 G1: 59.1 G2: 52.1	Yes	No
Gamito et al., 2010[141]	Unclear	Unclear	Unclear	No	No	No	90 80 100 100	No	No
Gersons et al., 2000[51]	Unclear	Unclear	No	Yes	No	No	98 100 95	No	No
Ghafoori et al., 2017[214]	Yes	Unclear	Yes	No	No	No	Overall: 30 G1: 33 G2: 28	Yes	No
Haller et al., 2016[145]	Unclear	Unclear	Yes	Unclear	No	No	Overall: 60.2 G1: 59.7 G2: 60.7	Yes	No
Hamner et al., 2003[83]	Unclear	Unclear	Yes	Yes	Yes	Yes	53 67	Yes	No
Hamner et al., 2009[215]	Unclear	Unclear	Yes	Yes	No	Unclear	56 46	Yes	No
Harned et al., 2014[144]	Unclear	Unclear	No	Yes	No	No	Overall: 69.2 G1: 66.7 G2: 70.6	Yes	No
Hensel-Dittmann et al., 2011[216]	Yes	Yes	No	No	No	No	75 73 77	Yes	No
Hertzberg et al., 1999[217]	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	93 91 100	No	No

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Hertzberg et al., 2000[178]	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	92 100 83	No	Yes
Hien et al., 2004[57]	Unclear	Unclear	Yes	Unclear	No	No	76 61 71 100	Yes	No

Table E-12. Risk of bias assessments, part 12

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Frommberger et al., 2004[212]	No	CA	Yes	Not Assessed	No	High
Galovski et al., 2012[6]	Yes	Mixed	Yes	Yes	Yes	Med
Galovski et al., 2016[213]	Yes	Unclear	Yes	Yes	Yes	High
Gamito et al., 2010[141]	No	CA	Yes	Not Assessed	No	Med
Gersons et al., 2000[51]	NR	Unclear	Yes	Not Assessed	Yes	Med
Ghafoori et al., 2017[214]	Yes	Other	Yes	Yes	Yes	High
Haller et al., 2016[145]	Unclear	Other	Yes	Yes	NA	Med
Hamner et al., 2003[83]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Hamner et al., 2009[215]	Yes	Other	Yes	Not Assessed	NA	High
Harned et al., 2014[144]	Yes	Mixed	Yes	Yes	Yes	Med
Hensel-Dittmann et al., 2011[216]	Yes	Mixed effects models	Yes	Not Assessed	No	High
Hertzberg et al., 1999[217]	No	CA	Mixed	Not Assessed	NA	High
Hertzberg et al., 2000[178]	No	Other	Mixed	Not Assessed	NA	High
Hien et al., 2004[57]	Yes	LOCF	Yes	Not Assessed	Yes	Med

Table E-13. Risk of bias assessments, part 13

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Hien et al., 2009[157] Hien et al., 2012[158]	Yes	Yes	Yes	Yes	No	No	1 week 63 61 64 3 mos. 63 58 12 mos. 63 59	Yes	No
Hinton et al., 2005[34]	Unclear	Unclear	Yes	Yes	No	No	100 100 100	No	No
Hinton et al., 2009[151]	Yes	Unclear	Yes	Yes	No	No	100 100 100	No	No
Hinton et al., 2011[152]	Unclear	Unclear	Yes	Unclear	No	Unclear	100 100 100	No	No
Hogberg et al., 2007[48]	Yes	Yes	Yes	Yes	No	No	88 92 82	No	No
Holliday et al., 2015[218]	Unclear	Unclear	No	Yes	No	No	Unclear	Yes	NR
Hollifield et al., 2007[32]	Yes	Yes	Yes	Yes	No	No	78 66 75	Yes	No
Ironson et al., 2002[219]	No	Unclear	No	No	No	No	73 50 100	Yes	Yes
Ivarsson, 2014[24]	Yes	Yes	Yes	Yes	No	No	Overall: 77.4 G1: 83.9 G2: 71.0	Yes	No

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Jiang et al., 2014[220]	No	No	No	No	No	No	Overall: 71 G1: 59 G2: 86	Yes	Yes
Johnson et al., 2006[221]	Unclear	Unclear	No	Yes	No	No	75 73 79	Yes	No
Johnson et al., 2011[29]	Yes	Unclear	No	No	No	No	91 97	No	No

Table E-14. Risk of bias assessments, part 14

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Hien et al., 2009[157] Hien et al., 2012[158]	Yes	Other	Yes	Not Assessed	Yes	Med
Hinton et al., 2005[34]	No	NA	Yes	Not Assessed	No	Med
Hinton et al., 2009[151]	No	NA	Yes	Not Assessed	No	Med
Hinton et al., 2011 [152]	No	NA	Yes	Not Assessed	No	Med
Hogberg et al., 2007[48]	No	CA	Yes	Not Assessed	Yes	Med
Holliday et al., 2015[218]	No	CA	Yes	Yes	No	High
Hollifield et al., 2007[32]	Yes	LOCF	Yes	Not Assessed	No	Med
Ironson et al., 2002[219]	No	CA	Yes	Not Assessed	No	High
Ivarsson et al., 2014[24]	Yes	Other	Yes	Yes	NA	Med
Jiang et al., 2014[220]	Yes	CA	No	Yes	No	High
Johnson et al., 2006[221]	No	CA	Yes	Not Assessed	No	High
Johnson et al., 2011[29]	Yes	Other	Yes	Not Assessed	Yes	Med

Table E-15. Risk of bias assessments, part 15

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Karatzias et al., 2011 [222]	Unclear	Unclear	Yes	Yes	No	No	59 57 61 F/U 50 48 52	Yes	No
Keane et al., 1989[223]	Unclear	Unclear	No	No	No	No	NR NR NR	NR	NR
Kearney et al., 2013[159]	Unclear	Yes	No	Yes	No	No	Overall: 93.6 G1: 95.5 G2: 92	No	No
Knaevelsrud et al., 2015[224]	Yes	Yes	No	No	No	No	Overall: 58.9 G1: 58.8 G2: 59	Yes	No
Krakow et al., 2000 [225]	Unclear	Unclear	Yes	Unclear	No	No	54 49 59	Yes	No
Krakow et al., 2001[52]	Yes	Unclear	Yes	Yes	No	No	68 61 75	Yes	No
Krupnick et al., 2008[226]	Unclear	Unclear	Unclear	Unclear	No	No	63 44	Yes	Yes
Krystal et al., 2011 [85]	Yes	Yes	Yes	Unclear	Yes	Yes	83 84 83	No	No
Kubany et al., 2003[35]	Unclear	Unclear	Yes	Yes	No	No	86 95 78	No	Yes

Table E-16. Risk of bias assessments, part 16

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Karatzias et al., 2011 [222]	Yes	Other	Yes	Not Assessed	Mixed	High
Keane et al., 1989[223]	NR	NR	No	Not Assessed	No	High
Kearney et al., 2013[159]	Yes	Unclear	Yes	Yes	No	Med
Knaevelsrud et al., 2015[224]	Yes	LOCF	Yes	Yes	No	High
Krakow et al., 2000 [225]	No	CA	Yes	Not Assessed	No	High
Krakow et al., 2001[52]	Yes	LOCF	Yes	Not Assessed	No	Med
Krupnick et al., 2008[226]	Yes	Other	Yes	Not Assessed	No	High
Krystal et al., 2011 [85]	Yes	MI	Yes	Not Assessed	NA	Low
Kubany et al., 2003[35]	Yes	LOCF	Yes	Not Assessed	No	Med

Table E-17. Risk of bias assessments, part 17

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Kubany et al., 2004[28]	Unclear	Unclear	Unclear	Yes	No	No	65 73 56	Yes	Yes
Langkaas et al., 2017[142]	Yes	Yes	Unclear	Yes	No	No	Overall: 82 G1: 82 G2: 82	No	No
Lee et al., 2002[227]	No	No	Unclear	No	No	No	89 NR NR	No	No
Li et al., 2017[172]	Yes	Yes	Yes	Yes	Yes	Yes	Overall: 90 G1: 89 G2: 92	No	No
Lindauer et al., 2005[50]	Yes	Yes	Yes	Yes	No	No	75 58 92	Yes	Yes
Lindley et al., 2007[228]	Unclear	Unclear	Yes	Yes	Yes	Yes	45 75	Yes	Yes
Littleton et al., 2016[229]	Yes	Unclear	Unclear	Unclear	No	No	Overall: 49.4 G1: 51.2 G2: 47.8	Yes	No
Litz et al., 2007[33]	Unclear	Unclear	Yes	Yes	No	No	73 Unclear Unclear	Yes	No
Maguen et al., 2017[25]	Unclear	Unclear	Yes	Unclear	No	No	Overall: 90.9 G1: 93.8 G2: 88.2	No	No

Table E-18. Risk of bias assessments, part 18

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Kubany et al., 2004[28]	Yes	Main analysis: CA Some from ITT analysis: LOCF	Yes	Not Assessed	No	Med
Langkaas et al., 2017[142#6049]	Yes	Unclear	Yes	Yes	Yes	Med
Lee et al., 2002[227]	NR	Unclear	Yes	Not Assessed	Yes	High
Li et al., 2017[172]	Yes	Unclear	Yes	Yes	NA	Low
Lindauer et al., 2005[50]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Lindley et al., 2007[228]	No	Unclear	Yes	Not Assessed	NA	High
Littleton et al., 2016[229]	Yes	MI	Yes	Yes	NA	High
Litz et al., 2007[33]	Yes	Other	Yes	Not Assessed	No	Med
Maguen et al., 2017[25]	No	NA	Yes	Yes	No	Med

Table E-19. Risk of bias assessments, part 19

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Marcus et al., 1997[230]	Yes	Unclear	NR	No	No	No	NR	NR	NR
Margolies et al., 2013[231]	Unclear	Unclear	Yes	Unclear	Unclear	Unclear	Overall: 75 G1: 70 G2: 80	Yes	No
Markowitz et al., 2015[132] Markowitz et al., 2016[135]	Yes	Unclear	No	Yes	No	No	Overall: 75 G1: 75 G2: 85 G3: 66	Yes	Yes
Marks et al., 1998[122] Lovell et al., 2001[123]	Yes	Unclear	No	Yes	No	No	89 87 95 79 95	No	Yes
Marshall et al., 2001[64]	Unclear	Unclear	Unclear	Unclear	Yes	Yes	63 65 61 64	Yes	No
Marshall et al., 2007[177]	Unclear	Unclear	Unclear	Yes	Yes	Yes	47 Unclear Unclear	Yes	Yes
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	Yes	Unclear	Yes	Unclear	Unclear	Yes	NR	NR	NR
Martenyi et al., 2007[62]	Unclear	Unclear	Yes	Yes	Unclear	Yes	86 90 88	No	No
Maxwell et al., 2016[124]	Yes	Unclear	Yes	Yes	No	No	Overall: 100 G1: 100 G2: 100	No	No

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
McDonagh et al., 2005[39]	Unclear	Unclear	Yes	Yes	No	No	67 59 91 91 77	Yes	Yes
McGovern et al., 2015[27]	Unclear	Yes	Yes	Yes	No	No	Overall: 78 G1: 73 G2: 81 G3: 80	Yes	No
McLay et al., 2011[232]	Unclear	Unclear	Unclear	Unclear	No	No	95 100 90	No	No
McRae et al., 2004[233]	Unclear	Unclear	Unclear	Unclear	Yes	Yes	70 68 72	Yes	No
Mills et al., 2012[20]	Yes	Yes	No	Yes	No	No	Overall: 71.8 G1: 67.3 G2: 77.1	Yes	Yes
Monnelly et al., 2003[167]	Unclear	Unclear	Unclear	Yes	Yes	Yes	88 100	No	No

Table E-20. Risk of bias assessments, part 20

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Marcus et al., 1997[230]	No	Other	Yes	Not Assessed	No	High
Margolies et al., 2013[231]	Yes	LOCF	Yes	Yes	NA	High
Markowitz et al., 2015[132] Markowitz et al., 2016[135]	Yes	MI	Yes	Yes	Yes	Med
Marks et al., 1998[122] Lovell et al., 2001[123]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Marshall et al., 2001[64]	Yes	LOCF	Yes	Not Assessed	NA	Med
Marshall et al., 2007[177]	Yes	Other	Yes	Not Assessed	NA	High
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	Yes	LOCF	Yes	Not Assessed	NA	Med
Martenyi et al., 2007[62]	Yes	LOCF	Yes	Not Assessed	NA	Med
Maxwell et al., 2016[124]	NA	NA	Yes	Yes	Yes	Med
McDonagh et al., 2005[39]	Yes	LOCF	Yes	Not Assessed	Yes	Med
McGovern et al., 2015[27]	Yes	Mixed	Yes	No	Yes	Med
McLay et al., 2011 [232]	No	CA	Mixed	Not Assessed	No	High
McRae et al., 2004[233]	No	None	Yes	Not Assessed	NA	High
Mills et al., 2012[20]	Yes	Other	Yes	Yes	Yes	Med
Monnelly et al., 2003[167]	No	CA	Yes	Not Assessed	NA	Med

Table E-21. Risk of bias assessments, part 21

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Monson et al., 2006[1]	Unclear	Unclear	Yes	Yes	No	No	83 80 87	No	No
Monson et al., 2012[22]	Yes	Yes	No	Yes	No	No	Overall: 77.5 G1: 85 G2: 70	Yes	Yes
Moradi et al., 2014[160]	Yes	Yes	Yes	Yes	No	No	Overall: 100 G1: 100 G2: 100	No	No
Morath et al., 2014[55]	Unclear	Unclear	No	Yes	No	No	Unclear	NR	NR
Mueser et al., 2008[7 391]	Yes	Yes	Yes	Yes	No	Yes	68 70 65	Yes	Yes
Mueser et al., 2015[234]	Yes	Yes	Yes	Yes	No	No	Overall: 75 at 6 mo G1: 70 G2: 79	Yes	No
Nacasch et al., 2011[15]	Unclear	Yes	Yes	Yes	No	No	87 87 87	No	No
Naylor et al., 2015[235]	Unclear	Unclear	No	Unclear	Yes	Yes	Overall: 75 G1: 87.5 G2: 62.5	Yes	Yes
Neuner et al., 2004[161]	Yes	Yes	Yes	Yes	No	No	93 88 93 100	No	No
Neuner et al., 2008[54]	No	Yes	Yes	Yes	No	No	91 96 80 100	Yes	Yes

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Neuner et al., 2010[53]	Unclear	Unclear	Yes	Yes	No	No	94 88 100	No	No
Nijdam et al., 2012[154]	Yes	Yes	Yes	Yes	No	No	64 60 69	Yes	No
Niles et al., 2012[236]	Yes	No	No	Unclear	No	No	Overall: 72.7 G1: 75 G2: 70.6	Yes	No
Noohi et al., 2017[237]	No	No	Unclear	No	No	No	NR	NR	NR
Panahi et al., 2011[71]	Yes	Unclear	Yes	Yes	Yes	Yes	89 91 86	No	No
Padala et al., 2006[238]	Unclear	Unclear	No	Unclear	Yes	Yes	75 82 67	Yes	Yes
Paunovic et al., 2001[239]	Unclear	Unclear	Unclear	No	No	No	80 89 73	Yes	Yes

Table E-22. Risk of bias assessments, part 22

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Monson et al., 2006[1]	Yes	Other	Yes	Not Assessed	Yes	Med
Monson et al., 2012[22]	Yes	Other	Yes	Yes	Yes	Med
Moradi et al., 2014[160]	No	NA	Yes	Yes	No	Med
Morath et al., 2014[55]	Yes	Mixed	Yes	Yes	No	Med
Mueser et al., 2008[7]	Yes	MI	Yes	Not Assessed	NR	Med
Mueser et al., 2015[234]	Unclear	Other	Yes	Yes	Mixed	High
Nacasch et al., 2011[15]	Yes	Unclear	Yes	Not Assessed	No	Med
Naylor et al., 2015[235]	Yes	LOCF	Yes	Yes	NA	High
Neuner et al., 2004[161]	Yes	Other	Yes	Not Assessed	Mixed	Med
Neuner et al., 2008[54]	Yes	Other	Yes	Not Assessed	Yes	Med
Neuner et al., 2010[53]	Yes	Other	Yes	Not Assessed	No	Med
Nijdam et al., 2012[154]	Yes	Mixed linear models	Yes	Not Assessed	Yes	Med
Niles et al., 2012[236]	No	NA	Yes	Yes	NA	High
Noohi et al., 2017[237]	No	Unclear	Yes	Yes	NA	High
Panahi et al., 2011[71]	Yes	LOCF & MI	Yes	Not Assessed	NA	Low
Padala et al., 2006[238]	No	CA	Yes	Not Assessed	NA	High
Paunovic et al., 2001[239]	NR	Unclear	Yes	Not Assessed	No	High

Table E-23. Risk of bias assessments, part 23

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Petrakis et al., 2012[185, 240]	Unclear	Yes	No	Yes	Yes	Yes	64 80 73 67	Yes	Yes
Petrakis et al., 2016[241]	Unclear	Unclear	Yes	Unclear	Unclear	Yes	Overall: 75/96 (78%) completed the study (i.e., had complete data at 12 weeks) G1: 43/50 (86%) G2: 32/46 (69.6%)	Yes	Yes
Polusny et al., 2015[136]	Yes	Unclear	No	Yes	No	No	Overall: 85.3 G1: 93.1 G2: 77.6	No	Yes
Popiel et al., 2015[242]	Unclear	Yes	Unclear	Yes	No	No	Post-treatment completers: Overall: 61 G1: 78 G2: 40 G3:46 Provided data at Followup (of randomized) Overall: 80% (182/228)	Yes	Yes
Power et al., 2002[243]	Yes	Yes	Yes	Yes	No	No	69 69 57 83	Yes	Yes
Raskind et al., 2003[74]	Unclear	Unclear	Unclear	Yes	Yes	Yes	100 60 (only 20% of those who received placebo 2nd completed)	Yes	Yes

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Raskind et al., 2007[75]	Yes	Unclear	Unclear	Yes	Yes	Yes	85 80 85	No	No
Raskind et al., 2013[76]	Unclear	Yes	Yes	Yes	Yes	Yes	Overall: 68.7 G1: 65.7 G2: 71.9	Yes	No
Rauch et al., 2009[244]	Unclear	Unclear	No	Yes	No	No	68 66 60 96	Yes	Yes
Rauch et al., 2015[245]	Unclear	Unclear	Unclear	Yes	No	No	Overall: 87 G1: 83.3 G2: 61.1	No	Yes
Ready et al., 2010[246]	Unclear	Unclear	No	Yes	No	No	82 83 80	No	No
Reger et al., 2016[18]	Yes	Unclear	Yes	Yes	No	No	Overall: 67.3 VRE: 55.6 PE: 59.3 WL: 87	Yes	Yes
Reich, 2005[84]	Unclear	Unclear	Yes	Unclear	Yes	Yes	76 75 78	Yes	No
Reist, 1989[181]	Unclear	Unclear	Unclear	Unclear	Unclear	Unclear	67 NR NR	Yes	NR
Resick, 2002[3] Resick, 2003[125] Resick et al., 2012[126]	Unclear	Unclear	Yes	Yes	No	No	67 66 65 85	Yes	Yes
Resick, 2015[127] Bryan, 2016[128]	Unclear	Unclear	Yes	Yes	No	No	Overall: 48.1 G1: 51.9 G2: 44.6	Yes	No

Table E-24. Risk of bias assessments, part 24

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid, and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Petrakis et al., 2012[185]	Yes	Other	Yes	Not Assessed	Yes	Med
Petrakis et al., 2016[241]	Yes	Unclear	Yes	Yes	NA	High
Polusny et al., 2015[136]	Yes	Other	Yes	Yes	NA	Med
Popiel et al., 2015[242]	Yes	CA	Yes	Yes	Mixed	High
Power et al., 2002[243]	No	CA	Yes	Not Assessed	No	High
Raskind et al., 2003[74]	No	LOCF	Yes	Not Assessed	NA	Med
Raskind et al., 2007[75]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Raskind et al., 2013[76]	Yes	Unclear	Yes	Yes	NA	Med
Rauch et al., 2009[244]	No	CA	Yes	Not Assessed	No	High
Rauch et al., 2015[245]	No	CA	Yes	Yes	No	High
Ready et al., 2010 [246]	No	CA	Yes	Not Assessed	No	High
Reger et al., 2016[18]	No	CA	Yes	Yes	Yes	Med
Reich, 2005[84]	Yes	LOCF	Yes	Not Assessed	NA	Med
Reist, 1989[181]	No	CA	No	Not Assessed	NA	High
Resick, 2002[3] Resick, 2003[125] Resick et al., 2012[126]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Resick, 2015[127] Bryan, 2016[128]	Yes	MI	Yes	Yes	Yes	Med

Table E-25. Risk of bias assessments, part 25

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Rosaura Polak, 2015[247]	Unclear	Unclear	Yes	Unclear	No	No	Overall: 100 G1: 100 G2: 100	No	No
Rothbaum, 1997[45]	Unclear	Unclear	No	Yes	No	No	86 NR NR	No	Unclear
Rothbaum, 2005[13]	Unclear	Unclear	No	Yes	No	No	81 NR NR NR	No	No
Rothbaum, 2008[248]	Unclear	Unclear	Yes	Unclear	Unclear	Yes	64 100	Yes	Yes
Ruglass et al., 2017 [143]	Unclear	No	No	Yes	No	No	Overall:65 G1: 64 G2: 53 G3: 86	Yes	Yes
Sannibale, 2013[146]	Yes	Yes	Yes	Yes	No	No	Overall: 75.8 G1: 72.4 G2: 78.8	Yes	No
Sautter, 2015[131]	Unclear	Unclear	Yes	Yes	No	No	Overall: 75 G1: 75 G2: 76	Yes	No
Schneier et al., 2015[249]	Unclear	Yes	Yes	Yes	Yes	Yes	Overall: 23.7 G1: 15 G2: 33	Yes	Yes
Schnurr, 2003[139]	Yes	Yes	Yes	Yes	No	No	84 77 91 Booster treatment 92 96 91	No	No
Schnurr, 2007[138]	Yes	Yes	Yes	Yes	No	No	71 62 79	Yes	Yes

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Schnyder, 2011[49]	Unclear	Unclear	No	Yes	No	No	93 94 93	Yes	No
Simon, 2008[174]	Unclear	Unclear	Yes	Yes	Yes	Yes	80 73 86	Yes	No
Simpson, 2015[250]	Unclear	Yes	No	Yes	Yes	Yes	G1: 85.7 G2: 45.5	Yes	Yes
Sloan et al., 2012[17]	Yes	Yes	Yes	Yes	No	No	Overall: 95.7 G1: 90.9 G2: 100	No	No
Sonne et al., 2016[186]	Yes	Yes	Yes	Yes	No	No	Overall: 75.4 G1: 69.4 G2: 80.7	Yes	No

Table E-26. Risk of bias assessments, part 26

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Rosaura Polak, 2015[247]	No	Other	Yes	Yes	No	High
Rothbaum, 1997[45]	No	Unclear	Yes	Not Assessed	Yes	Med
Rothbaum, 2005[13]	No	CA	Yes	Not Assessed	Yes	Med
Rothbaum, 2008[248]	No	CA	Yes	Not Assessed	NA	High
Ruglass et al., 2017 [143]	Yes	Unclear	Yes	Yes	Yes	Med
Sannibale, 2013[146]	Yes	Other	Yes	Yes	Yes	Low
Sautter, 2015[131]	Yes	Mixed	Yes	Yes	Yes	Med
Schneier et al., 2015[249]	Yes	Unclear	Yes	Yes	NA	High
Schnurr, 2003[139]	Yes	Other	Yes	Not Assessed	Yes	Low
Schnurr, 2007[138]	Yes	MI	Yes	Not Assessed	Yes	Med
Schnyder, 2011[49]	Yes	LOCF	Yes	Not Assessed	Yes	Med
Simon, 2008[174]	Yes	LOCF	Yes	Not Assessed	No	Med
Simpson, 2015[250]	Yes	Unclear	Yes	No	NA	High
Sloan et al., 2012[17]	No	NA	Yes	Yes	Yes	Low
Sonne et al., 2016[186]	Yes	Mixed	Yes	Yes	NA	Med

Table E-27. Risk of bias assessments, part 27

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Spence, 2011[30]	Yes	Unclear	No	No	Unclear	No	81 78 86	No	No
Stecker, 2014[251]	Yes	Unclear	No	Unclear	No	No	Overall: 79.3 G1: 82.2 G2: 76.2	Yes	No
Stein, 2002[80]	Unclear	Unclear	Yes	Yes	Yes	Yes	70 78	Yes	No
Stenmark, 2013[252]	No	Unclear	Yes	No	No	No	Overall: 67 G1: 65 G2: 70	Yes	No
Suris, 2013[253]	Yes	Unclear	Yes	Yes	No	No	Overall: 48.1 G1: 49.1 G2: 47.2	Yes	No
Tarrier, 1999[129] Tarrier, 1999[130]	Yes	Yes	No	Yes	No	No	86 83 89	No	No
Taylor, 2003[133]	Unclear	Unclear	Yes	Yes	Yes	No	75 68 79 79	Yes	No
ter Heide, 2016[43]	Yes	Yes	No	Yes	No	No	Overall: 80.6 G1: 77.8 G2: 83.3	No	No
Tucker, 2001[65]	Unclear	Unclear	Yes	Unclear	Unclear	Yes	61 62 60	Yes	No
Tucker, 2003[175] Tucker, 2004[176]	Unclear	Unclear	Yes	Yes	Yes	Yes	76 80 74 70	Yes	No
Tucker, 2007[78]	Yes	Yes	Yes	Yes	Unclear	Yes	74 84	Yes	No

Table E-28. Risk of bias assessments, part 28

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
Ulmer, 2011[254]	Unclear	Unclear	Yes	No	No	Unclear	82 67 100	No	Yes
van den Berg, 2015[16]	Yes	Yes	Yes	Yes	No	No	Overall: 78.7 G1: 83.0 G2: 78.2 G3: 75.5	No	No
van der Kolk, 1994[63]	Unclear	Unclear	Unclear	Unclear	Unclear	Yes	73 64 87	Yes	Yes
van der Kolk, 2007[47]	Unclear	Unclear	Yes	Yes	Yes	Yes	83 87 90	No	No
van der Kolk, 2016[162]	Yes	Unclear	Yes	Yes	No	No	Overall: 84.6 G1: 91.7 G2: 78.6	No	No

Table E-29. Risk of bias assessments, part 29

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
Spence, 2011[30]	Yes	Other	Yes	Not Assessed	No	Med
Stecker, 2014[251]	No	Other	Yes	Yes	No	High
Stein, 2002[80]	Yes	LOCF	Yes	Not Assessed	NA	Med
Stenmark, 2013[252]	Yes	Other	Yes	Yes	No	High
Suris, 2013[253]	Yes	Other	Yes	Yes	No	High
Tarrier, 1999[129] Tarrier, 1999[130]	No	CA	Yes	Not Assessed	Yes	Med
Taylor, 2003[133]	No	CA	Yes	Not Assessed	Yes	Med
ter Heide, 2016[43]	Yes	MI	Yes	Yes	Yes	Low
Tucker, 2001[65]	Yes	LOCF	Yes	Not Assessed	NA	Med
Tucker, 2003[175] Tucker, 2004[176]	No	LOCF	Yes	Not Assessed	NA	Med
Tucker, 2007[78]	Yes	LOCF	Yes	Not Assessed	NA	Med
Ulmer, 2011[254]	Yes	Other	Yes	Not Assessed	No	High
van den Berg, 2015[16]	Yes	Mixed	Yes	Yes	Yes	Low
van der Kolk, 1994[63]	No	CA	Yes	Not Assessed	NA	Med
van der Kolk, 2007[47]	Yes	LOCF	Yes	Not Assessed	NA	Med
van der Kolk, 2016[162]	Yes	Other	Yes	Yes	NA	Med

Table E-30. Risk of bias assessments, part 30

Author, Year	Was randomization adequate?	Was allocation concealment adequate?	Were groups similar at baseline?	Were outcome assessors masked?	Were care providers masked?	Were patients masked?	% Completed Treatment G1 G2 G3 G4	Was overall attrition ≥20%?	Was differential attrition ≥15%?
van Emmerik, 2008[40]	Yes	Yes	Yes	Yes	No	No	68 NR NR	Yes	No
Vera et al., 2011[255]	Unclear	Unclear	No	Unclear	No	Unclear	Overall: 83 G1: 71 G2: 100	No	Yes
Villarreal et al., 2016[256]	Yes	Unclear	No	Unclear	Unclear	Yes	Completed Study Overall: 47/80 (59%) G1: 29/42 (69%) G2: 18/38 (47%)	Yes	Yes
Wagner, 2007[257]	Unclear	Unclear	No	Yes	No	No	88 75 100	No	No
Wahbeh et al., 2016[258]	Yes	Yes	Yes	No	No	No	Unclear	NR	NR
Wells, 2014[19]	Yes	Yes	No	No	No	No	Overall: 93.8 G1: 100 G2: 90.9 G3:90.9	No	No
Yeh, 2011[79]	Yes	Yes	No	Yes	Yes	Yes	74 82 67	Yes	Yes
Zlotnick, 1997[259]	Unclear	Unclear	No	No	No	No	69 71 67	Yes	No
Zlotnick, 2009[56]	Unclear	Unclear	No	No	No	No	90 85 95	No	No
Zohar, 2002[72]	Unclear	Unclear	No	Yes	Yes	Yes	74 79	Yes	No

Table E-31. Risk of bias assessments, part 31

Author, Year	Did the study use ITT analyses?	Method of Handling Dropouts	Were outcome measures equal, valid and reliable?	Were all prespecified outcomes reported?	Did study report adequate treatment fidelity based on measurement by independent raters?	Risk of Bias Rating
van Emmerik, 2008[40]	Yes	LOCF	Yes	Not Assessed	No	Med
Vera et al., 2011[255]	No	CA	Yes	Yes	No	High
Villarreal et al., 2016[256]	Yes	LOCF	Yes	Yes	NA	High
Wagner, 2007[257]	Yes	LOCF	Yes	Not Assessed	No	High
Wahbeh et al., 2016[258]	No	CA	Yes	Yes	No	High
Wells, 2014[19]	No	CA	Yes	Yes	Yes	Med
Yeh, 2011[79]	No	LOCF	Yes	Not Assessed	NA	Med
Zlotnick, 1997[259]	No	CA	Mixed	Not Assessed	No	High
Zlotnick, 2009[56]	No	CA	Yes	Not Assessed	No	Med
Zohar, 2002[72]	Yes	Unclear	Yes	Not Assessed	Yes	Med

CA = Completer Analyses; G = group; ITT = intent-to-treat; LOCF = Last Observation Carried Forward; Med = Medium; MI = Multiple Imputation; NA = not applicable; NR = not reported.

Additional Comments on Studies Rated High Risk of Bias

Ahmadizadeh et al., 2013:[198] No details about randomization, blinding, completion of treatment, fidelity, how dropouts were handled in analyses.

Arntz et al., 2007:[199] Very high attrition and high differential attrition (just 45% completed in one group, 72% in the other); outcome assessor and randomization procedures unclear; outcome assessors not described as masked; no description of treatment fidelity.

Beck et al., 2009:[200] High risk of attrition bias, due to the overall and the differential attrition (24% difference between groups). Unclear whether groups were similar at baseline for demographics and most potential confounders (as the information is not provided). In addition, inadequate handling of missing data (used completers analysis). No description of randomization method or allocation concealment.

Beidel et al., 2011:[201] High risk of selection bias; completers analysis in a small trial (N=35) with high differential dropout; and risk of bias from no masking.

Bichescu et al., 2007:[202] No attempt to create similar groups, this subsequently affected assessor blinding. Few details of randomization process beyond "were randomized".

Braun et al., 1990:[169] High attrition, non-standard outcome measures, baseline data not reported to allow determination of similarity or differences between groups.

Brom et al., 1989:[203] Appears to be completers analysis with no approach to handling missing data reported; no data reported to allow comparison of groups at baseline; no masking of outcome assessors reported; no information on treatment fidelity; methods of randomization and allocation concealment not reported; potential measurement bias due to differences in timing of assessments across groups.

Butollo et al., 2016:[204] Very large loss to followup, do not know details about randomization or allocation concealment or outcome assessor masking, fidelity reported as tested but details not provided on adequacy. Self-report primary outcomes.

Davidson et al., 1993:[180] Davidson, 1990:[179] Completer analysis for all subjects completing minimum of 4 weeks (40/46 subjects did so and were included in the analyses, 87%); and separately for the 33/46 (71.1%) that completed 8 weeks; no treatment of missing data; with high attrition. It was also unclear whether randomization or allocation concealment were adequate.

Davis et al., 2004:[205] Very high attrition (close to 50% overall); groups mostly similar at baseline but differed in prior treatments (with just 1 subject in the placebo group previously treated with an antidepressant vs. 15 to 27% of subjects with previous treatment with antidepressants, benzodiazepines, or other medication in the nefazodone group); ITT analysis with LOCF (with exception of 1 patient).

Difede et al., 2007:[206] Very high attrition, and high differential attrition; over 1/2 for the CBT group did not complete treatment.

Dorrepaal et al., 2012:[207] Groups differ by those with adult abuse and trauma severity scores, and analyses did not adjust for these baseline differences. Outcome assessors of primary outcomes not blinded because they are self-reported. Only secondary outcome assessors were blinded. Randomization methods not reported, no fidelity details given. Providers and patients not masked.

Dunne et al., 2012:[208] No randomization or allocation concealment details, text states that outcome assessors were not blinded.

Feske et al., 2008:[209] High risk of selection bias and confounding; already small sample size and the high overall and differential attrition with completer analysis; attrition bias; 4 of 13 randomized subjects in the prolonged exposure group (31%) dropped out, 2 were withdrawn due to medication changes and 2 for unknown reasons; 2/14 treatment as usual clients withdrawn.

Foa et al., 1991:[210] High attrition for some groups and high differential attrition; completer analysis only; study did not report adequate treatment fidelity; some baseline differences between groups for income, assault characteristics; high risk of selection bias and confounding.

Franklin et al., 2017:[211] Could not determine whether groups were similar at baseline, large loss to followup, completer analysis.

Frommberger et al., 2004:[212] High risk of selection bias and confounding; attrition bias; no reporting of adequate fidelity; Small sample size with no data shown on baseline covariates across groups; outcome assessment not masked; over 20% attrition and nothing done for missing data (completer analysis).

Galovski et al., 2016:[213] Unclear whether patients and providers were blinded. High overall attrition.

Ghafoori et al., 2017:[214] Differences in race at baseline, but probably ok; large loss to followup, outcome assessors not blind to treatment allocation.

Hamner et al., 2009:[215] Substantial dropout, limited description of randomization; study reported as double blind, but write up suggests VPA folks got a lot more blood draws/monitoring; also, study physician told by pharmacist to adjust doses, so not blind to treatment arm.

Hensel-Dittman et al., 2011:[216] High risk of selection bias and confounding. First, no data were reported to allow baseline comparison of groups for most variables, and this is a fairly small sample size, making baseline differences more likely. The authors only report baseline data for a few of the outcome measures, and there was an 11-point difference between groups for baseline CAPS score. They did some matching during the randomization, but it is unclear if that worked to produce comparable groups at baseline. Next, the study did not report adequate treatment fidelity based on measurement by independent raters; no information was reported about

treatment fidelity. They report that they videotaped all sessions, but there is no information reported to confirm to support adequate treatment fidelity, which would be very important since all of the same therapists delivered both interventions and it would be fairly easy to have some of the components of one therapy introduced into the other therapy. Next, lack of masking; the authors report that they attempted to keep outcome assessors blind, but that treatment condition was occasionally revealed to them, but it is unclear how frequently this occurred.

Hertzberg et al., 1999:[217] Baseline characteristics not reported for important potential confounders in this small study (n =15) to allow for determination of potential selection bias; in addition, unclear whether randomization or allocation concealment were adequate; unclear whether outcome assessors were masked. Completers analysis.

Hertzberg et al., 2000:[178] Baseline characteristics not reported for important potential confounders in this small study (n=12) to allow for determination of potential selection bias (described as "non-significant difference", but given small sample size, almost any difference will be non-significant). In addition, unclear whether randomization or allocation concealment were adequate; unclear whether outcome assessors were masked. Instruments of uncertain validity used to assess outcomes.

Ironson et al., 2002:[219] High risk of selection bias; randomization compromised by adding more participants to PE group to achieve equal group numbers; high overall and differential attrition (and 50% dropouts from the PE group); marked differences in baseline severity of PTSD and depression between groups (otherwise, minimal baseline data reported to allow comparison of groups); completer analysis; no handling of missing data.

Jiang et al., 2014:[260] Very high attrition and differential attrition. Small study so no one could be masked, main outcome measures not validated in Chinese population. Fidelity reported as assessed but findings not reported.

Johnson et al., 2006:[221] Inadequate methods of handling missing data, completers analysis; did not report adequate treatment fidelity based on measurement by independent raters; high potential for selection bias with small numbers in each treatment arm and no reporting of baseline demographics (only reported in aggregate for the three intervention groups) and potential confounders for comparison, and there were differences in the baseline values for the measures of PTSD symptoms (e.g., baseline CAPS scores were 82 for Counting and 61.7 for EMDR, 64.2 for waitlist). The authors describe the study as a randomized trial. However, from their description of the design, it appears that the participants for the waitlist control group were recruited separately from the group recruited to the active treatments. In other words, participants recruited to the active condition were randomized to one of three active treatments, but the persons recruited to the control condition were not assigned to that group randomly. Accordingly, it's not really a randomized trial for the comparisons with the control condition.

Karatzias et al., 2011:[222] Very high attrition rate (over 40%); unclear whether randomization or allocation concealment were adequate.

Keane et al., 1989:[223] High risk of selection bias: Baseline differences between groups included race (for Intervention vs. waitlist: 0% vs. 31% Black), and service connection (36% vs. 69%) possibly biasing control group toward reporting greater severity of symptoms; difference between group in co-interventions/medications administered over the course of the study (42.9% [6/14] in intervention group received anxiolytic, sleep, or pain meds at some point during the study vs. 76.9% [10/13] in the control group received anxiolytic medications at some point during waiting; and some evidence suggests worse outcomes for those with PTSD treated with anxiolytics). The PTSD ratings were completed by therapists who were administering the therapy and thus were not blinded. Of note, the study found no difference between active intervention and control group in self-reported PTSD symptoms but a substantial difference in PTSD ratings completed by the non-blinded therapists. Potential measurement bias with no masking or independence of outcome assessors and outcomes assessed at different timepoints for the two groups. Unclear whether randomization, allocation concealment, and masking were adequate. Attrition information not reported, nor was approach to handling missing data. No description of methods to ensure treatment fidelity.

Knaevelsrud et al., 2015:[224] No blinding, very large loss to followup, no adherence assessed.

Krakow et al., 2000:[225] Very high attrition, around 50%; did not report adequate treatment fidelity.

Krupnick et al., 2008:[226] High risk of selection bias due to attrition. Very high attrition and high differential attrition (% completers by group: 63 vs. 44). Regarding "other" method of handling dropouts: imputed missing scores as the application of the observed group mean change.

Lee et al., 2002:[227] Inadequate randomization procedure (alternating); no allocation concealment, no blinding of outcome assessors; unclear whether groups were similar at baseline for several characteristics; details of analysis and missing data were NR; differential attrition data unclear.

Lindley et al., 2007:[228] High attrition and high differential attrition (30%), method of handling dropouts/missing data was unclear.

Littleton et al., 2016:[229] Very high attrition, allocation concealment unclear, masking unclear of outcome assessors.

Marcus et al., 1997:[230] No data reported to allow assessment of how groups compare at baseline, how many patients dropped out after randomization, or how many people are in the 2 groups. Attrition information not reported; does not describe use of ITT analysis; Outcome assessors were not masked, increasing potential for measurement bias; did not report adequate treatment fidelity.

Margolies et al., 2013:[231] Unclear randomization, allocation concealment, and all blinding, large overall attrition, fidelity not assessed.

Marshall et al., 2007:[177] High risk of selection bias due to high rate of attrition. Also, not clear if groups were similar at baseline (article does not show the data--it just has a sentence that says

that patient demographics did not differ significantly between groups; although later Tables do show similar baseline PTSD severity for CAPS and some other measures).

McLay et al., 2011:[232] Unclear adequacy of randomization or allocation concealment; unclear whether or not outcome assessors were masked; small sample with possible significant differences in prior deployments between treatment groups, raising risk of selection bias. The measures themselves were reliable but post assessments were reported to be given sporadically over a 36-week period. Study did not report adequate treatment fidelity.

McRae et al., 2004:[233] Completers analysis with inadequate handling of missing data in this head-to-head study that found no difference between treatments; high risk of selection bias; unable to determine if randomized groups were similar at baseline (data only reported for completers; 26/37 subjects); unclear whether randomization and allocation concealment were adequate.

Mueser et al., 2015:[234] High attrition and, for some time points, differential attrition. Reported percent completion at 6 months because that was the lowest percent assessed in each group but did not account for treatment engagement.

Naylor et al., 2015:[235] No randomization details presented, high attrition and differential attrition, baseline differences not accounted for in analyses, small sample sizes.

Niles et al., 2012:[236] Providers and patients only masked until the end of the first assessment; Therapist compliance is mentioned but details are not presented; Unclear about outcome assessor blinding; Did not account for dropouts in analysis.

Noohi et al., 2017:[237] This is a very small study (n-=30) with virtually no information reported to allow us to assess risk of bias. The authors say the participants were randomized but no other information was provided; no masking information was reported, no loss to followup data, no information about how missing data were handled, etc.

Padala et al., 2006:[238] High risk of selection bias and confounding; differential attrition along with small sample size (N=20); completer analysis; only reports age, race, mean TOP-8, and mean CAPS at baseline---the race characteristics were quite different (55% Caucasian in Risperidone group vs. 89% in the Placebo group).

Paunovic et al., 2001:[239] High risk of selection bias and confounding; high differential attrition in this small (N=20) head to head study comparing two types of psychotherapy that found no difference between the two, and was not powered to find a small to moderate difference between treatments; no assessor masking; did not reported whether ITT; handling of missing data not reported.

Petrakis et al., 2016:[241] Randomization methods/allocation concealment/masking are all unclear in the text; authors state it is a double-blind study but do not provide details. Only 56% of patients remained on study medication for 12 weeks (40% in G1, 48% in G2). Authors do not explain how dropouts/missing data are handled in analyses. Consort table reports that 100% of

randomized patients received allocated intervention but results text suggests that 1 patient randomized to placebo reported wrong medication being dispensed. Additionally, 1 patient randomized to placebo reported that the "medication blind" envelope was not properly filed. Poor quality is due to high attrition and low treatment completion rate as well as unclear randomization/concealment/masking methods. Of note is that results may not be generalizable to outpatient settings since a majority of the participants were in a residential substance use program.

Popiel et al., 2015:[242] High attrition, nearly 50% of paroxetine group refused to participate in assigned treatment.

Power et al., 2002:[243] High overall and differential attrition; completers analysis; no approach to handling missing data; no assessment of treatment fidelity; in the two active treatment groups, about 31% and 43% did not complete treatment, respectively.

Rauch et al., 2009:[244] High risk of selection bias and confounding; completers analysis, using just the set of subjects that completed an RCT (Foa et al 2005, J Consul Clin Psychol); baseline differences in race and income.

Rauch et al., 2015:[245] No randomization or allocation concealment details reported, patients and providers not masked, large differential attrition, no information on baseline group differences, no accounting for those lost to followup, no fidelity assessment.

Ready et al., 2010:[246] High risk of selection bias and confounding. This small study (N = 11) did not report differences in many baseline covariates across intervention groups. However, there were large differences in some of the few that they did report (CAPS, BDI), which strongly suggests that there were important differences in baseline covariates.

Reist et al., 1989:[181] Non-standard outcome measures, high attrition, only overall attrition not group-specific attrition reported, completer analysis.

Rosaura Polak, 2015:[247] Very small n=8 pilot study with unclear randomization, allocation concealment, assessor blinding, and fidelity.

Rothbaum et al., 2008:[248] Randomization unclear, high differential attrition (36% differential), completer's analysis; unclear whether outcome assessor were masked.

Schneier et al., 2015:[249] Very high attrition, randomization unclear.

Simpson, 2015:[250] Attrition reported for original 12 week treatment period. During the course of the study, the investigators decided to stop the study at 6 weeks because they were concerned about the study length. Randomization also unclear.

Stecker, 2014:[251] Unknown whether allocation concealment or blinding of outcome assessors occurred; no fidelity assessed; large loss to followup; analyses not done on ITT basis and did not

account for attrition; no provider and patient masking; and all information collected was self-report.

Stenmark, 2013:[252] Randomization method was drawing balls from a bag (presumably no allocation concealment). Baseline characteristics similar for gender, age, months in exile and region of origin; no characteristics reported for comorbidity, length of PTSD or other clinical factors. Authors used therapists from other centers to assess diagnostic status and symptom severity; attempts were made at blinding, but at least 20% of patients revealed treatment information to assessors. Percent completed treatment refers to those who completed 1 month and 6-month post-treatment testing and was high; authors report ITT analyses but exact method for addressing missing outcome data unclear.

Suris, 2013:[253] A therapist had really poor fidelity so the authors removed all participants counseled by that therapist, resulting in very high loss to followup of randomized sample. Even so, the analyzed sample still had substantial loss to followup and differential loss to followup. Allocation concealment not clear and no blinding of patients or providers.

Ulmer et al., 2011:[254] High risk of selection bias and confounding in this small study (N=22); differential attrition (% completers: 82 vs. 67 vs. 100); no description of treatment fidelity; unclear adequacy of randomization and allocation concealment; no masking of outcome assessors. Also, participants received a range of treatments outside of the study varying in intensity and type.

Vera et al., 2011:[255] Very small (n=14) study. No information about randomization, allocation concealment, or masking of outcome assessors or patients. Differential attrition. Baseline CAPS scores significantly higher for usual care group than PE group. No ITT analysis done. No treatment fidelity reported (although therapists were supervised).

Villarreal et al., 2016:[256] Large attrition and differential attrition. Baseline differences between groups (although authors adjusted for those variables in analyses). Also, the paper says it is a double-blind trial but authors do not describe who was masked to allocation.

Wagner et al., 2007:[257] High risk of selection bias and confounding in this small study (N=8) with randomization method unclear, and groups different at baseline (younger in treatment group: mean age 28 vs. 39; more males 75% vs. 0%; more prior trauma and greater injury severity); no description of treatment fidelity; single therapist.

Wahbeh et al., 2016:[258] Loss to followup not reported; outcome assessors not blinded; completer analysis only; no fidelity measure.

Zlotnick et al., 1997:[259] High attrition (31%) with completers analysis; no masking of outcome assessors; baseline data not reported to allow comparison of groups for many things (they did run statistical tests for some demographic variables, and report no statistically significant differences); higher baseline scores for DTS, CR-PTSD, and DES for the wait list group.

Appendix F. Study Characteristics and Findings

Table F-1. Clinician administered PTSD scales, self-administered PTSD scales, remission, and loss of PTSD diagnosis

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Acarturk et al., 2016[44]	G1: EMDR-R-TEP G2: WL	HTQ Mean (SE at pre-tx; SD at post-tx and followup) G1 Pre-tx:2.63 (13.65) G1 Post-tx: 1.42 (0.07) G1 1 month FU: 1.57 (0.08) G2 Pre-tx: 2.47 (0.43) G2 Post-tx: 2.38 (0.08) G2 1 month FU: 2.38 (0.08) G1 vs G2 pre to post-tx p<0.001 G1 vs G2 pre-tx to FU, p<0.001 Treatment X Time, F = 1.33, p = 0.254 from post-tx to FU Mean estimated difference, post-tx: -0.96 (95% CI, -1.18 to -0.74), p <0.001 Mean estimated difference, 1 month FU: -0.81 (95% CI, -1.04 to -0.58), p <0.001	IES-R Mean (SE at pre-tx; SD at post-tx and followup) G1 Pre-tx:59.69 (13.65) G1 Post-tx:21.36 (2.76) G1 1 month FU: 25.87 (3.01) G2 Pre-tx: 62.55 (12.46) G2 Post-tx: 59.01 (2.92) G2 1 month FU: 60.37 (3.01) G1 vs G2 pre to post-tx p<0.001 G1 vs G2 pre-tx to FU p<0.001 Treatment X Time, F = 0.50, p = 0.483 from post-tx to FU Mean estimated difference, post-tx: -37.65 (95% CI, -45.66 to 29.63), p <0.001 Mean estimated difference, 1 month FU: -34.50 (95% CI, -43.25 to -25.76), p <0.001	Remission NR Loss of Diagnosis based on MINI PTSD, n (%) G1 Post-tx: 30 (61) G2 Post-tx: 3 (6) X^2 (df) = 33.31 (1), p <0.001 OR = 24.21 (95% CI, 6.59 to 88.98) NNT=2 (95%CI, 1.4-2.5) G1 1 month followup: 24 (49) G2 1 month followup: 2 (4) X^2 (df) = 25.34 (1), p <0.001 X^2 (df) = 25.34 (1), p <0.001 OR = 22.56 (95% CI, 4.92 to 103.35) NNT=3 (95% CI, 1.9-5.7)

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Acosta et al., 2017[149]	G1: Web CBT plus TAU (Thinking Forward and usual VA primary care services) G2: TAU, usual VA primary care services	NR	PCL Treatment by time interaction effect, NS for PTSD severity and PTSD symptoms during in-treatment period, Estimate: -0.09 (0.50) Treatment by time effect, NS for PTSD severity and PTSD symptoms contrasting in and post treatment period (period between post treatment and 3 month followup), Estimate: 0.40 (0.82)	Remission Clinically meaningful improvement on PCL PTSD symptoms (i.e., >10-point decrease) 12 weeks G1:41.0% G2: 31.3% Chi-square, NS 3-month followup G1: 37.5% G2: 29.7% Chi-square, NS No longer reporting clinical levels of distress based on PCL distress (i.e., >50) 12 weeks G1: 22.2% G2: 17.9% Chi-square, NS 3-month followup G1: 17.9% G2: 23.4% Chi-square, NS Loss of Diagnosis: NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Akuchekian et al., 2004[77]	G1: Topiramate 25 to 500 mg/day (sensitive patients started at 12.5mg/day) G2: Placebo	CAPS Mean (SD) G1 Pre-tx: 50.70 (7.7) G1 Post-tx: 32.75 (8.2) G2 Pre-tx: 48.9 (9.13) G2 Post-tx: 46.62 (8.8) G1 vs. G2, p=0.00 (based on t-test)	NR	NR NR
Asukai et al., 2010[10]	G1: CBT, exposure-based therapy G2: UC	CAPS Adjusted Mean (SE) G1 Pre-tx:84.58 (7.78) G1 Post-tx: 43.76 (8.43) G2 Pre-tx:84.33 (7.78) G2 Post-tx: 84.81 (7.96) At post: G1 vs. G2= p<0.01(based on t-test)	IES-R Adjusted Means (SE) G1 Pre-tx: 59.67 (5.06) G1 Post-tx: 21.15 (5.53) G2 Pre-tx: 59.75 (5.06) G2 Post-tx: 53.75 (5.20) At post: G1 vs. G2 = p<0.001 (based on t-test)	NR NR
Bartzokis et al., 2005[86]	G1: Risperidone 1 to 3 mg/day G2: Placebo	CAPS Unadjusted Change from baseline (SD) G1: -14.3 (16.7) G2: -4.6 (13.2) G1 vs. G2, p<0.05	NR	NR NR
Basoglu et al., 2007[11]	G1: CBT, exposure-based therapy G2: WL	CAPS Mean (SD) G1 Pre-tx: 63.1 (10.1) G1 Week 4: 38.7 (18.7) G1 Week 8:30.2 (20.3) G2 Pre-tx: 62.3 (14.5) G2 Week 4: 54.5 (16.9) G2 Week 8: 49.1 (20.3) G1 vs. G2 at Week 4, p<0.01 G1 vs. G2 at Week 8, p<0.01	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Batki et al., 2014[165]	G1: Topiramate 25 to 300mg G2: Placebo	NR	PCL total Between-group analysis Weeks 1 to 12 Avg. G1: 42.3 (16.0) G2: 49.0 (16.5) P p = 0.100, IRR = -9.01, 95% CI -19.8-1.80, % diff. = 14 Main Effects of treatment, F (1,48) = 2.81, p = 0.100	Remission NR Loss of PTSD diagnosis NR
Becker et al., 2007[183]	G1: Bupropion 100 to 300 mg/day G2: Placebo	CAPS Within-Group Mean Change (SD)(Baseline-Endpoint) G1: 12.33 (24.12) G2: 16.99 (11.26) Group effect, p<0.01	DTS Within-Group Mean Change (SD)(Baseline-Endpoint) G1: 13.22 (21.62) G2: 10.6 (29.20) Group effect, p<0.05	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Blanchard et al., 2003[36]	G1: CBT-mixed G2: Supportive psychotherapy G3: WL	CAPS Mean (SD) G1 Pre-tx: 68.2 (22.7) G1 Post-tx: 23.7 (26.2) G2 Pre-tx: 65.0 (25.9) G2 Post-tx:40.1 (25.7) G3 Baseline: 65.8 (26.6) G3 Post-tx: 54.0 (25.9) Group X Time at post-tx, p<0.001 G1 vs. G2, p=0.002 G1 vs. G3, p<0.001 G2 vs. G3, p=0.012 Including Dropouts Group X Time at post-tx, p<0.001 G1 vs. G2, p=0.013 G1 vs. G3, p<0.001 G2 vs. G3, p=0.052 Group X Time, 3 mth FU p=0.048 G1 continued to have lower scores than G2, p=0.003 Decreases from post-tx to the 3 mth fu, NS	IES Mean (SD) G1 Baseline: 40.4 (13.8) G1 Post-tx: 12.1 (14.9) G1 FU: 12.2 (13.6) G2 Baseline: 38.7 (20.9) G2 Post-tx: 27.4 (19.1) G2 FU: 24.0 (20.1) G3 Baseline:40.2 (15.9) G3 Post-tx: 36.6 (17.2) Post-tx G1 vs. G2 & G3, p<0.01 G2 vs. G3, NS PCL Mean (SD) G1 Baseline: 54.4 (12.2) G1 Post-tx: 31.3 (14.1) G1 FU: 31.1 (14.2) G2 Baseline: 55.0 (14.7) G2 Post-tx: 43.8 (14.6) G2 FU: 40.8 (14.4) G3 Baseline: 55.9 (13.3) G3 Post-tx: 53.9 (14.1) Post-tx G1 vs. G2 & G3, p<0.01 G2 vs. G3, significantly greater change	NR Improved from PTSD to sub-syndromal PTSD or non-PTSD G1: 76.2% G2: 47.6 G3: 23.8% 3 month FU G1: 81% G2: 42.9%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Boden et al., 2012[58]	G1: Seeking Safety and TAU G2: TAU	NR	IES-R Mean (SD) G1 Pre-tx: 46.8 (19.5) G1 Post-tx: 40.8 (20.9) G1 6 mth FU: 38.9 (16.7) G2 Pre-tx: 47.4 (16.3) G2 Post-tx: 42.4 (21.3) G2 6 mth FU: 36.5 (16.9) Between Group Differences, NS G1 Within-Group Differences Pre-tx vs. 6mth FU, p<0.05 G2 Within-Group Differences Pre-tx vs. 6mth, p<0.05 G2 Within-Group Differences Post-tx vs. 6 mth FU, p<0.05	NR NR
Bohus et al., 2013[23]	G1: DBT-PTSD G2: TAU-WL	CAPS Mean (SD) G1 Pre-tx: 87.92 (14.20) G1 Post-tx: 60.31(26.76) G1 18 week followup: 57.47 (25.66) G1 24 week followup: 58.50 (24.20) G2 Pre-tx: 82.63 (18.20) G2 Post-tx: 83.53 (16.50) G2 18 week followup: 79.74 (21.67) G2 24 week followup: 80.21 (19.21) Hedges' g between group: 1.35 Treatment X Time Interaction: -1.138 (0.195), p<0.001	PDS Mean (SD) G1 Pre-tx: 2.22 (0.44) G1 Post-tx: 1.61 (0.64) G1 18 week followup: 1.53 (0.55) G1 24 week followup: 1.53 (0.65) G2 Pre-tx: 2.09 (0.45) G2 Post-tx: 2.09 (0.46) G2 18 week followup: 2.05 (0.47) G2 24 week followup: 2.00 (0.42) Hedges' g between group: 1.00 Treatment X Time Interaction: -0.021 (0.006), p<0.001	Remission: NR Loss of Diagnosis at 12 weeks weeks (not meeting DSM-IV PTSD criteria any longer according to the CAPS) G1: 14 (38.9%) G2: 4 (10.5%) p=0.0018 Borderline Personality Disorder Subgroup G1: 7 (41.2%) G2: 0 (0.0%) p=0.0058

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Brady et al., 2000[66]	G1: Sertraline 25 to 200 mg/day G2: Placebo	CAPS-2 Mean change (SEM) G1: -33.0 (2.8) G2: -23.2 (2.9) Difference Between Mean Change (95% CI): 9.8 (1.8 to 17.7), p=0.02	IES Mean Change (SEM) G1: -16.2 (1.6) G2: -12.1 (1.6) Difference Between Mean Change (95% CI): 4.1 (-0.4 to 8.7), p=0.07 DTS Mean Change (SEM) G1: -28.1 (2.8) G2: -16.1(2.8) G1 vs. G2 p=0.003	NR NR
Brady et al., 2005[67]	G1: Sertraline 150 mg/day G2: Placebo	CAPS ANCOVA F (2, 68) = 2.68, p=0.08	IES Authors reported 'no significant difference between groups' (data NR)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Bryant et al., 2003[41]	G1: CBT, exposure based therapy (Prolonged Imaginal Exposure) G2: CBT-Mixed Prolonged Imaginal Exposure plus Cognitive Restructuring G3: Supportive Control	CAPS-Intensity Mean (SD) G1 Pre-tx: 32.50 (8.71) G1 Post-tx: 19.15 (11.15) G1 6 mth FU: -20.70 (12.00) G2 Pre-tx: 32.70 (7.51) G2 Post-tx: 15.90 (13.36) G2 6 mth FU: 15.70 (14.79) G3 Pre-tx: 32.83 (8.01) G3 Post-tx: 28.00 (15.31) G3 6 mth FU: 30.28 (12.89) Post-tx, p<0.01 (main effects) FU, p<0.05 (main effects) CAPS-Frequency (CAPS-F) Mean (SD) G1 Pre-tx: 36.80 (9.82) G2 Post-tx: 20.55 (12.73) G1 6 mth FU: 23.25 (12.90) G2 Pre-tx: 36.00 (8.69) G2 Post-tx:17.20 (15.62) G2 6 mth FU: 17.00 (15.22) G3 Pre-tx: 38.33 (9.64) G3 Post-tx: 30.00 (16.42) G3 6 mth FU: 32.44 (13.57) Post-tx, p<0.01 (main effects) FU, p<0.05 (main effects)	IES-Intrusions Mean (SD) G1 Pre-tx: 23.85 (7.07) G1 Post-tx: 17.65 (7.34) G1 6 mth FU: 17.60 (9.88) G2 Pre-tx: 26.60 (7.02) G2 Post-tx:15.10 (12.86) G2 6 mth FU: 15.95 (12.18) G3 Pre-tx: 28.44 (6.60) G3 Post-tx: 15.10 (12.86) G3 6 mth FU: 25.44 (7.79) Post-tx, p<0.01 (main effects) FU, p<0.05 (main effects) IES-Avoidance Mean (SD) G1 Pre-tx: 26.40 (6.65) G1 Post-tx: 19.45 (13.48) G1 6 mth FU: 20.75 (12.66) G2 Pre-tx: 26.40 (6.65) G2 Post-tx: 16.15 (13.49) G2 6 mth FU: 14.95 (12.32) G3 Pre-tx: 26.17 (8.95) G3 Post-tx: 25.50 (9.54) G3 6 mth FU: 24.78 (9.55) Post-tx, p<0.01 (main effect) FU, p<0.05 (main effect)	NR No longer met criteria for PTSD at Posttreatment G1: 50.0% G2: 65.0% G3: 33.0% p(G2/G3) <0.05 No longer met criteria for PTSD at 6 month followup G1: 50.0% G2: 60.0% G3: 22.0% p(G1/G3) <0.07 p(G2/G3) <0.05

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Bryant et al., 2008[42]	G1: CBT, exposure based (Imaginal Exposure) G2: CBT, exposure-based therapy (In vivo exposure) G3: CBT, exposure-based therapy (Imaginal Exposure/In vivo Exposure) G4: CBT-mixed Imaginal Exposure/In vivo Exposure/ cognitive restructuring	CAPS Mean (SD) G1 Pre-tx: 73.29 (18.82) G1 Post-tx: 55.50 (33.83) G1 6 mth FU: 59.94 (32.36) G2 Pre-tx: 76.79 (15.53) G2 Post-tx: 55.96 (24.56) G2 6 mth FU: 59.32 (29.62) G3 Pre-tx: 76.06 (19.19) G3 Post-tx: 55.39 (37.45) G3 6 mth FU: 56.39 (35.87) G4 Pre-tx: 71.35 (17.28) G4 Post-tx: 29.86 (27.11) G4 6 mth FU: 32.86 (27.44) Post-tx, p<0.01 (main effect) 6 mth FU, p<0.005 (main effect)	IES-Intrusions, Mean (SD) G1 Pre-tx: 24.48 (7.56) G1 Post-tx:19.94 (8.62) G1 6 mth FU: 20.87 (10.40) G2 Pre-tx: 24.21 (10.55) G2 Post-tx:17.25 (11.83) G2 6 mth FU: 19.21 (12.58) G3 Pre-tx: 27.58 (8.72) G3 Post-tx: 20.81 (13.17) G3 6 mth FU: 23.05 (12.14) G4 Pre-tx: 24.89 (8.01) G4 Post-tx: 14.07 (10.58) G4 6 mth FU: 13.35 (11.01) Post-tx, NS (main effect) 6 month FU, p<0.05 (main effect) IES-Avoidance, Mean (SD) G1 Pre-tx: 29.10 (6.03) G1 Post-tx: 20.58 (11.52) G1 6 mth FU: 21.13 (10.56) G2 Pre-tx: 22.68 (10.52) G2 Post-tx:17.54 (12.29) G2 6 mth FU: 17.57 (10.85) G3 Pre-tx: 27.61 (8.50) G3 Post-tx: 21.81 (14.31) G3 6 mth FU: 25.16 (15.14) G4 Pre-tx: 23.71 (8.63) G4 Post-tx:13.14 (11.00) G4 6 mth FU: 13.18 (12.58) Post-tx, NS (main effect) 6 month FU, p<0.05 (main effect)	NR No PTSD at Posttreatment (Based on CAPS) G1: 37.0% G2: 35.0% G3: 41.0% G4: 65.0% p<0.10 No PTSD at 6 month followup (Based on CAPS) G1: 25.0% G2: 31.0% G3: 37.0% G4: 69.0% p<0.01

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Butterfield et al., 2001[82]	G1: Olanzapine 5 to 20mg/day G2: Placebo	SIP Mean (SD) G1 Pre-tx: 39.7 (9.7) G1 Post-tx: 19.2 (8.7) G2 Pre-tx: 45.9 (8.2) G2 Post-tx: 17.0 (17.5) TOP-8 Mean (SD) G1 Pre-tx: 19.3 (4.2) G1 Post-tx: 12.6 (6.4) G2Baseline: 21.8 (3.3) G2 Post-tx: 10.5 (8.7) SPRINT - Mean (SD) G1 Pre-tx: 31.5 (5.7) G2 Post-tx: 17.9 (7.8) G2 Pre-tx: 34.8 (2.1) G2 Post-tx: 20.5 (11.1)	DTS Mean (SD) G1 Pre-tx: 91.6 (25.4) G1 Post-tx: 57.4 (35.6) G2 Pre-tx: 95.8 (16.7) G2 Post-tx: 56.0 (36.6) G1 vs. G2, no group X time differences found	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Carey et al., 2012[81]	G1: Olanzapine 5 to 10mg G2: Placebo	CAPS Mean (SD) G1 Pre-tx: 79.4 (16) G1 Post-tx 4 week: 49.1 (27.2) G1 Post-tx 8 week: 33.6 (28.2) % CAPS score reduced: 57.7% G2 Pre-tx: 81.6 (11.3) G2 Post-tx 4 week: 73.21 (20.5) G1 G2 Post-tx 8 week: 62.3 (31.9) % CAPS score reduced: 23.7% Week 4 G1 vs G2, p = 0.014 Week 8 G1 vs. G2, p = 0.018, Effect size, r = 0.43 Response (>50% reduction in CAPS score) G1: 71% G2: 21%	DTS Mean (SD) G1 Pre-tx: 75 (16.3) G1 Post-tx 4 week: 54.8 (27.7) G1 Post-tx 8 week 8: 37.9 (32) % CAPS score reduced: 51% G2 Pre-tx: 88.1 (22.5) G2 Post-tx 4 week: 86.2 (22.3) G1 Post-tx 8 week: 75.8 (34.5) % CAPS score reduced: 16% Week 4 G1 vs G2, p = 0.003 Week 8 G1 vs. G2, p = 0.006, Effect size, r = 0.5	CGI severity Mean (SD) G1 Pre-tx: 4.7 (0.8) G1 Post-tx 8 week: 2.9 (1.4) G2 Pre-tx: 5 (0.8) G1 Post-tx 8 week: 4.1 (1.3) Week 8 G1 vs. G2, p = 0.027, Effect size, r = 0.4 Response (CGI improvement scale=much or very much improved) G1: 11 (78.6%) G2: 4 (28.6%) Loss of PTSD diagnosis NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Carlson et al., 1998[46]	G1: EMDR G2: CBT, coping skills therapy (Biofeedback and general relaxation) G3: WL	CAPS - Frequency Mean (SD) G1 Pre-tx: 2.5 (0.5) G1 3 mth FU: 0.7 (0.6) G2 Pre-tx: 2.6 (0.5) G2 3 mth FU: 2.0 (0.7) G3 Pre-tx: 2.4 (0.6) NR Group X Time, p<0.0004 CAPS Total - Intensity: Mean(SD) G1 Pre-tx: 2.4 (0.7) G1 3 mth FU: 0.8 (0.7) G2 Pre-tx: 2.4 (0.5) G2 3 mth FU: 2.0 (0.5) G3 Pre-tx: 2.5 (0.6) NR Group X Time, p<0.002 CAPS Total - Overall Mean Change (SD) at 9 months G1: 36.9 (28.6) G2: 67.8 (24.7) p<0.05	IES Total Mean (SD) G1 Pre-tx: 52.5 (9.0) G1 Post-tx: 35.2 (22.0) G1 3 mth: 29.1 (22.0) G1 9 mth: 34.8 (28.0) G2 Pre-tx: 52.9 (9.3) G2 Post-tx: 44.5 (17.4) G2 3 mth: 45.7 (15.0) G2 9 mth: 47.0 (23.0) G3 Pre-tx: 52.8 (11.5) G3 Post-tx: 38.7 (16.2) Post-tx & 3 mth FU, Group X Time, p=NS 9 month FU, p<0.24 (t-test) MISS Mean (SD) G1 Pre-tx: 117.5 (14.3) G1 Post-tx: 92.8 (20.8) G1 3 mth: 92.4 (17.2) G1 9 mth: 97.8 (29.8) G2 Pre-tx: 119.4 (18.3) G2 Post-tx: 114.2 (17.5) G2 3 mth: 110.6 (18.6) G1 9 mth: 127.0 (12.4) G3 Pre-tx: 117.9 (17.6) G3 Post-tx: 112.9 (21.7)	NR PTSD diagnosis by CAPS at 3 months followup: G1: 77.8% (7 of 9) G2: 22.2% (2 of 9)

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Carlson et al., 1998[46] (continued)			Group X Treatment, p<0.006 G1 vs. G3, p<0.05 (post-tx) G1 vs. G2, p<0.05 (post-tx & followup) 3 month FU, p<0.05 (t-test) 9 month FU, p<0.05 (t-test)	
Chard et al., 2005[2]	G1: CBT, cognitive processing therapy CPT-SA G2: WL	CAPS-SX G1 Pre-tx: 65.46 (26.39) G1 Post-tx: 9.00 (11.04) G2 Pre-tx 68.30 (23.67) G2 Post-tx: 62.96 (30.68) p<0.001 (interaction)	MPSS Mean (SD) G1 Pre-tx: 57.57 (22.85) G1 Post-tx: 7.54 (9.51) G2 Pre-tx: 57.52 (24.74) G2 Post-tx: 57.70 (27.47) p<0.001 (interaction)	NR No longer met PTSD criteria based on CAPS-SX at Posttreatment G1: 93% G2: 26% p<0.001
Church et al., 2013[155]	G1: EFT, Emotional Freedom Techniques (brief exposure therapy combining cognitive and somatic elements, on PTSD and psychological distress symptoms in veterans) G2: WL	NR	PCL-M Mean (SE) G1 Pre-tx: 62.01 (2.1) G1 Post-tx: 39.41 (2.7) G2 Pre-tx: 62.71 (2.3) G2 Post-tx: 63.23 (2.0) Treatment X Time Interaction, <0.0001	NR NR
Cloitre et al., 2002[37]	G1: CBT, exposure-based therapy(STAIR) G2: WL	CAPS Mean (SD) G1 Pre-tx:69 (16.3) G1 Post-tx: 31 (25.2) G2 Pre-tx:69 (16.6) G2 Post-tx:62 (22.7) p<.01 (interaction)	MPSS-SR Mean (SD) G1 Pre-tx: 69 (16.6) G1 Post-tx: 29 (27.6) G2 Pre-tx:73 (18.6) G2 Post-tx:58 (28.6) p<0.01 (interaction)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Cloitre et al., 2010[148]	G1: CBT-Mixed (STAIR) + PE G2: CBT-Mixed (STAIR) + Support (Skills Training) G3: Support (Skills Training) + PE	CAPS Mean (SD) G1 Pre-tx:63.08 (18.29) G1 Post-tx: 32.70 (19.37) G1 3 mth FU:24.66 (18.47) G1 6 mth FU:20.44 (19.01) G2 Pre-tx: 64.34 (21.15) G2 Post-tx: 32.32 (23.04) G2 3 mth FU:31.88 (22.98) G2 6 mth FU:32.51 (22.69) G3 Pre-tx: 64.50 (15.86) G3 Post-tx: 39.72 (18.34) G3 3 mth FU: 39.71 (17.59) G3 6 mth FU: 28.56 (21.00) Group X Time G1 vs. G3 at 3 mths, p=0.01 No other contrasts significant	PSS-SR Mean (SD) G1 Pre-tx e:36.7 (12.87) G1 Post-tx: 14.0 (11.46) G1 3 mth FU:12.5 (11.41) G1 6 mth FU: 8.9 (9.83) G2 Pre-tx:39.9 (12.65) G2 Post-tx: 14.5 (12.79) G2 3 mth FU:17.3 (10.10) G2 6 mth FU: 13.7 (13.64) G3 Pre-tx: 38.2 (11.14) G3 Post-tx: 19.0 (9.83) G3 3 mth FU:21.4 (11.54) G3 6 mth FU: 20.5 (13.56) p=0.03(interaction) G1 pre vs. G1 post: p<0.001 G1 pre vs. G1 3 mon: p<0.001 G1 post to G1 6 mon: p<0.001	PTSD-negative @ posttreatment G1: 61% G2: 47% G3: 33% p=0.11 Persistence of PTSD-negative status (maintained their status through the 3-month and 6-months assessments) G1: 55% G2: 37% G3: 21% p=0.03 G1 vs G3: p=0.01 OR (95% CI):4.23 (1.42–12.59) CAPS score <20 at posttreatment G1: 27% G2: 24% G3: 6% p=0.04 Remission Rate: (Pairwise analyses) G1 vs. G3: p=0.04 OR (95% CI): 5.67 (1.11–28.81). The rate of sustained PTSD full remission differed among the three groups G1: 24%, G2: 13% G3: 0% p=0.002

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Coffey et al., 2016[140]	G1: Modified PE+ Motivational enhancement therapy (met-ptsd), G2: PE as described in G1 without MET, relaxation prior to PE therapy. G3: HLS, relaxation prior to PE therapy	NR	IES-R Mean (95% CI) G1 Pre-tx: 54.95 (49.51 to 60.39) G1 Post-tx: 20.49 (14.77 to 26.20) (p= 0.04) G1 3 month followup: 19.10(13.01 to 25.18) (p = 0.03) G1 6 month followup: 20.48 (14.53 to 26.42) (p < 0.05) G2 Pre-tx: 48.56 (43.43 to 53.68) G2 Post-tx: 16.20 (10.48 to 21.92) (p = 0.008) G2 3 month followup: 14.11(8.33 to 19.90) (p = 0.02) G2 6 month followup: 16.45 (10.85 to 22.06) (p = 0.13) G3 Pre-tx: 51.02 (45.65 to 56.60) G3 Post-tx: 27.40 (21.80 to 33.01) G3 3 month followup: 26.00 (20.15 to 31.85) G3 6 month followup: 26.50 (20.52 to 32.50) *p-values in parentheses denote the treatment in comparison with G3 Treatment x time interaction, post-tx: X^2 = 7.25, p = 0.03 Difference in score reduction at post-tx, G1 vs. G2, p = 0.55 Treatment X Time Interaction, followup: X^2 = 0.32, p = 0.32, p = 0.99 Cohen's d as compared with G3: G1 Post-tx: 0.36 G2 Post-tx: 0.62 G1 3 month: 0.36 G2 3 month: 0.65 G1 6 month: 0.31 G2 6 month: 0.55	NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171]	G1: Fluoxetine 10 to 60 mg/day G2: Placebo	SIP Week 12 difference (Baseline - Endpoint) (95% CI) G1 vs. G2 difference: 10.3 (3.7 to 16.9), p<0.005 According to Meltzer-Brody paper, effect was significant for all 4 cluster scores (p<0.02) (intrusion, avoidance, numbing, hyperarousal) Duke Global Severity Rating for PTSD (Duke) Week 12 difference (Baseline - Endpoint) (95% CI) G1 vs. G2 Difference: 1.1 (0.6 to 1.6), p<0.0001	DTS Week 12 difference (Baseline - Endpoint) (95% CI) G1 vs. G2 Difference: 27.4 (11.2 to 43.5), p<0.005 According to Meltzer-Brody paper, effect was significant (p<0.02) for all 4 cluster scores (intrusion, avoidance, numbing, hyperarousal)	NR NR
Cook et al., 2010[156]	G1: CBT, exposure-based therapy G2: Psychoeducation	CAPS Mean (SD) G1 Pre-tx: 81.34 (14.00) G1 Post-tx: 74.04 (20.36) G2 Pre-tx: 79.48 (15.27) G2 Post-tx:74.85 (19.52) p<0.001 (treatment effect, Wald)	PTSD Military Checklist Mean (SD) G1 Pre-tx: 62.73 (10.18) G1 1 mth:58.83 (13.56) G1 3 mth FU: 60.13 (12.16) G1 6 mth FU: 59.05 (11.78) G2 Baseline:65.06 (9.48) G2 1 mth:60.96 (11.43) G2 3 mth FU:61.13 (12.00) G2 6 mth FU: 59.64 (12.30) Interactions, NS	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Cottraux, 2008[31]	G1: CBT-mixed (Exposure in imagination or in vivo and cognitive therapy) G2: Supportive Control	NR	PCLS <44 (criteria for loss of PTSD diagnosis) (Post-tx): G1: 33% G2: 14% Fisher's exact, p=0.12 PCLS <35 (Post-tx) G1: 20% G2: 7% Fisher's exact, p=0.25 PCLS, mean change (SD): Mean change in G1: -13.5 (13.2) Mean change in G2: -6.3 (12.9) Group Effect, p=0.044 Interaction, NS	NR Proportion without PTSD at posttest: G1+G2 > G3, chi-sq = 10.58, df = 2, p=0.01
Davidson et al., 2001[68]	G1: Sertraline 50 to 200 mg/day G2: Placebo	CAPS-2 Change from Baseline to Endpoint (SD) G1: -33.0 (2.4) G2: -26.2 (2.3) p=0.04 (t-test)	IES Change from Baseline to Endpoint (SD) G1: -19.2 (1.5) G2: -14.1 (1.5) p=0.02 (t-test) DTS Change from Baseline to Endpoint (SD) G1: -32.3 (2.8) G2: -20.0 (2.7) p=0.002 (t-test)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Davidson et al., 2003[184]	G1: Mirtazapine 15 to 45 mg/day G2: Placebo	SIP Mean (SD) G1 Pre-tx:34.7 (7.0) G1 Post-tx:17.4 (4.0) G2 Pre-tx:38.4 (6.7) G2 Post-tx:32.9 (12.7) Between Tx effect size 1.06 p=0.04 Treatment effect F=5.0; p=.04) SPRINT Mean (SD) G1 Pre-tx:21.7 (6.0) G1 Post-tx:12.4 (8.8) G2 Pre-tx:25.0 (4.2) G2 Post-tx: 19.4 (8.2) Between Tx effect size 0.49 p=NS Treatment effect, F=1.7; p=.20	DTS Mean (SD) G1 Pre-tx: 74.8 (36.5) G1 Post-tx: 54.1 (40.0) Change: 20.7 G2 Pre-tx: 93.8 (29.4) G2 Post-tx: 82.6 (27.7) Change: 11.2 Treatment effect, p=0.20	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Davidson et al., 2006[69]	G1: Venlafaxine 75 to 300mg/day G2: Sertraline 50 to 200mg/day G3: Placebo	CAPS-SX17 Mean Within-group difference (95% CI): G1: -41.51 (-45.66 to -37.36) G2: -39.44 (-43.67 to - 35.21) G3: -34.17 (-38.33 to -30.01) Between group p-values based on pairwise comparisons from the analysis of covariance model using baseline adjusted values G1 vs. G3: 0.015 G2 vs. G3: 0.081 G1 vs. G2: 0.494	DTS Mean Within-group difference (95% CI): G1: -42.86 (-47.56 to -38.17) G2: -38.92 (-43.69 to -34.16) G3: -34.59 (-39.27 to -29.91) Between group p-values based on pairwise comparisons from the analysis of covariance model using baseline adjusted values G1 v G3: 0.015 G2 v G3: 0.203 G1 v G2: 0.248	CAPS-SX17 total ≤ 20 Scores reported in figure G1 vs. G3: p<0.05 at week 4 & 12 G1 vs. G2: p<0.01 at week 4, <0.05 at week 6 G1 vs. G3: p<0.001 at week 6 NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Davidson et al., 2006[73]	G1: Venlafaxine 37.5 to 300 mg/day G2: Placebo	CAPS-SX Mean (SD) G1 Pre-tx: 81.0 (14.62) G1 Post-tx: 29.2 (26.09) G2 Pre-tx: 82.9 (15.50) G2 Post-tx: 38.1 (29.11) Between Group Mean Difference -8.9, p=0.006	NR	Remission Rates at 12 weeks (score ≤ 20 on CAPS-SX) G1: 42.9% (n=69/161) G2: 28.0% (n=47/168) p=0.005 Remission Rates at 24 weeks (score ≤ 20 on CAPS-SX) G1: 50.9% (n=82/161) G2: 37.5% (n=63/168) p=0.01 NR
Davidson et al., 2007[166]	G1: Tiagabine 4 to16mg/day G2: Placebo	CAPS Change from baseline (SD) G1: 30.7 (25.1) G2: 30.2 (26.3) p=0.85 DTS & TOP-8 NR, both NS	NR	G1: 16% G2: 14% p=0.88 NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Davis et al., 2008[164]	G1: Divalproex 1000 to 3000 mg/day G2: Placebo	CAPS Mean(SD) G1 Pre-tx: 75.2 (19.1) G1 Post-tx: 60.1 (24.1) G2 Pre-tx: 77.3 (15.3) G2 Post-tx: 60.8 (26.6) 30% reduction in PTSD scores: G1: NR G2: NR Diff b/t groups, p>0.45 G1 vs. G2, diff over time, p=NS TOP-8 Mean(SD) G1 Pre-tx: 19.4 (5.3) G1 Post-tx: 15.4 (6.6) G2 Pre-tx: 19.7 (4.3) G2 Post-tx: 15.8 (6.5) G1 vs. G2, NS	DTS Data Not Presented G1 vs. G2, NS	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ehlers et al., 2003[5]	G1: CT G2: Self-help booklet based on principles of CBT G3: Repeated assessments	CAPS Frequency Mean (SD) G1 Pre-tx: 31.7 (9.5) G1 3 mth FU: 11.2(10.3) G1 9 mth FU: 10.2 (9.9) G2 Pre-tx: 32.6 (8.6) G2 3 mth FU: 22.9 (12.9) G2 9 mth FU: 21.4 (11.4) G3 Pre-tx: 32.8 (11.5) G3 3 mth FU: 25.6 (12.9) G3 9 mth FU: 21.1 (15.2) 3 mth FU Overall: p<0.001 G1 vs. G2, p<0.001 G1 vs. G3, p<0.001 9 mth FU Overall: p<0.001 G1 vs. G2: p<0.001 G1 vs. G3: p=0.001 CAPS Intensity Mean (SD) G1 Pre-tx: 26.7 (7.4) G1 3 mth FU: 10.2 (9.4) G1 9 mth FU: 9.7 (9.5) G2 Pre-tx: 26.7 (7.4) G2 3 mth FU: 19.6 (9.0) 18.6 (10.1) G2 9 mth FU: G3: 22.4 (11.9)	PDS Frequency Mean (SD) G1 Pre-tx: 30.2 (7.9) G1 3 mth FU: 8.3 (9.8) G1 9 mth FU: 8.7 (8.1) G2 Pre-tx: 30.9 (7.5) G2 3 mth FU: 19.9 (7.8) G2 9 mth FU: 20.0 (7.8) G3 Pre-tx: 31.1 (7.5) G3 3 mth FU: 22.6 (11.6) G3 9 mth FU: 19.4 (12.5) 3 mth FU Overall: p<0.001 G1 vs. G2, p<0.001 G1 vs. G3, p<0.001 9 mth FU Overall: p <0.001 G1 vs. G2, p<0.001 G1 vs. G3, p<0.001 PDS Distress Mean (SD) G1 Pre-tx: 31.6 (9.1) G1 3mth FU: 7.1 (10.3) G1 9 mth FU: 7.3 (8.6) G2 Pre-tx: 32.0 (7.2) G2 3 mth FU: 20.3 (8.2) G2 9 mth FU: 19.0 (8.8)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ehlers et al., 2003[5] (continued)		G3 Pre-tx: 25.9 (10.4) G3 3 mth FU: 22.4 (11.9) G3 9 mth FU: 17.0 (13.8) 3 mth FU Overall: p <0.001 G1 vs.G2: p<0.001 G1 vs. G3: p<0.001 9 mth FU Overall, p=0.002 G1 vs.G2, p=0.001 G1 vs. G3, p=0.004	G3 Pre-tx: 31.4 (8.4) G3 3 mth FU: 22.3 (12.2) G3 9 mth FU: 20.0 (14.1) 3mth FU Overall: p<0.001 G1 vs. G2: p<0.001 G1 vs. G3: p<0.001 9 mth FU Overall: p <0.001 G1 vs. G2, <0.001 G1 vs. G3, <0.001	
Ehlers et al., 2005[8]	G1: CBT-mixed Cognitive therapy including restructuring and exposure G2: WL	CAPS-Intensity Mean (SD) G1 Pre-tx: 36.5 (9.4) G1 Post-tx: 13.7 (13.4) G1 Post-tx FU adjusted: 10.4 G1 6 mth FU: 15.5 (14.8) G2 Pre-tx: 29.0 (8.5) G2 Post-tx: 30.9 (9.6) G2 Post-tx adjusted: 34.2 G1 vs. G2, p<0.005 Changes in G1, p<0.005 Changes in G2, NS CAPS-Frequency Mean (SD) G1 Pre-tx: 42.0 (8.5) G1 Post-tx: 16.0 (15.3) G1 Post-tx adjusted: 11.4 G1 6 mth FU: 16.0 (14.4)	PDS Mean (SD) G1 Pre-tx: 32.4 (6.5) G1 Post-txt: 10.3 (8.9) G1 6 mth FU: 12.4 (9.9) G2 Pre-tx: 31.2 (6.3) G2 Post-txt: 29.8 (8.4) G1 vs. G2, p<0.0005 Changes in G1, p<0.0005 Changes in G1, NS	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ehlers et al., 2005[8] (continued)		G2 Pre-tx: 31.6 (8.4) G2 Post-tx: 35.5 (11.4) G2 Post-tx adjusted: 40.2 G1 vs. G2, p<0.005 Changes in G1, p<0.005 Changes in G2, NS		
Ehlers et al., 2014[9]	G1: Intensive CT (standard CT delivered over a much shorter period) G2: Standard CT G3: Supportive Therapy G4: WL	CAPS Mean (SD) G1 Pre-tx: 78.72 (19.80) G1 Post-tx: 32.22 (27.20) G1 Followup 1 (27 weeks): 35.56 (26.26) G1 Followup 2 (40 weeks):35.33(35.11) Within-group pre-post effect, d= 1.95 G2 Pre-tx: 70.60 (13.45) G2 Post-tx: 26.97 (28.68) G2 Followup 1 (27 weeks): 20.86 (25.23) G2 Followup 2 (40 weeks): 20.96 (27.71) Within-group pre-post effect, d = 1.95 G3 Pre-tx: 74.60 (15.39) G3 Post-tx: 47.88 (31.77) G3 Followup 1 (27 weeks):49.32(32.46) G3 Followup 2 (40 weeks): 49.04 (38.01) Within-group pre-post effect, d = 1.07	PDS Mean (SD) G1 Pre-tx: 33.21 (7.66) G1 6 weeks: 14.85(8.92) G1 Post-tx:11.98 (9.60) G1 Followup 1 (27 weeks): 13.91 (11.63) G1 Followup 2 (40 weeks):13.03(13.99) Within-group pre-post effect, d= 2.45 G2 Pre-tx: 32.44 (6.94) G2 6 weeks: 16.33 (11.58) G2 Post-tx: 9.39 (10.88) G2 Followup 1 (27 weeks): 10.15 (11.86) G2 Followup 2 (40 weeks): 9.63 (11.26) Within-group pre-post effect, d = 2.53 G3 Pre-tx: 34.26 (7.40) G3 6 weeks: 23.30 (12.90) G3 Post-tx: 19.98 (13.67) G3 Followup 1 (27 weeks):18.93(12.98) G3 Followup 2 (40 weeks): 20.94 (15.40) Within-group pre-post effect, d = 1.30 G4 Pre-tx: 32.46 (7.60) G4 6 weeks: 31.92 (6.84) G4 Post-tx: 29.24 (9.36) Within-group pre-post effect, d = 0.38	Total Remission (no symptoms according to CAPS), n (%) G1 Post-tx:14 (46.7) G2 Post-tx:16 (51.6) G3 Post-tx:6 (20.0) G4 Post-tx: 1 (3.3) Greater remission in G1 and G2 vs. G3 X2 = 22.19, p<0.001 G1 Followup 1 (27 weeks):12 (40.0) G2 Followup 1 (27 weeks):21 (67.7) G3 Followup 1 (27 weeks):5 (16.7) Greater remission in G1 and G2 vs. G3 X2 = 16.41, p<0.001 G1 Followup 2 (40 weeks):16 (53.3) G2 Followup 2 (40 weeks):23 (74.2) G3 Followup 2 (40 weeks):8 (26.7) Greater remission in G1 and G2 vs. G3 X2 = 13.84, p<0.01 G1 NNT: 1.50 (95% 1.18 to 2.06) G2 NNT: 1.41 (95% 1.14 to 1.87) G3 NNT: 2.73 (95% 1.77 to 5.95)

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ehlers et al., 2014[9] (continued)		G4 Pre-tx: 69.95 (14.17) G4 Post-tx: 65.28 (20.64) Within-group pre-post effect, d = 0.26 Comparison of Treatment with Waitlist Treatment by time Interactions, F=21.50, df=3, 135.35, p<0.002 Between group effect sizes Adjusted Difference (95% CI) G1 vs. G4: -39.55 (26.60 to 52.51), p<0.001, d = 1.57 G2 vs. G4: -38.80 (26.19 to 51.40), p<0.001, d= 1.55 G1 vs. G3: -18.72(5.96 to 31.45), p <0.01, d=0.75 G2 vs G3: -17.96 (5.31 to 30.62), p<0.01, d = 0.72 Interaction between condition and Linear time effects: F=7.83, df=2, 154.13, p<0.001	Comparison of Treatment with Waitlist Treatment by time Interactions, F=21.16, df=3, 106.56, p<0.002 Between group effect sizes Adjusted Difference (95% CI) G1 vs. G4: 17.72 (12.54 to 22.90), p<0.001, d = 1.75 G2 vs. G4:19.84 (14.71 to 24.97), p<0.001, d= 1.96 G1 vs. G3: 7.37(2.19 to 12.55), p <0.01, d=0.73 G2 vs G3: 17.96 (5.31 to 30.62), p<0.01, d = 0.72 Interaction between condition and Linear time effects: F=4.42, df=2, 215.14, p = 0.01	Loss of Diagnosis (CAPS, patient no longer met the minimum number of symptoms in each symptom cluster) required by DSM-IV,), n (%) G1 Post-tx:22 (73.3) G2 Post-tx:24 (77.4) G3 Post-tx:13 (43.3) G4 Post-tx: 2 (6.7) Greater loss of diagnosis in G1 and G2 vs. G3 X2 = 38.92, p<0.001 G1 Followup 1 (27 weeks):22 (73.3) G2 Followup 1 (27 weeks):23 (74.2) G3 Followup 1 (27 weeks):11 (36.7) Greater loss of diagnosis in G1 and G2 vs. G3 X2 = 11.70, p<0.01 G1 Followup 2 (40 weeks):20 (66.7) G2 Followup 2 (40 weeks):23 (74.2) G3 Followup 2 (40 weeks):12 (40.0) Greater loss of diagnosis in G1 and G2 vs. G3 X2 = 8.18, p<0.05

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Engel et al., 2015[26]	G1: DESTRESS-PC, a nurse guided online CBT and stress inoculation training. G2: Optimized Usual Care, usual primary care PTSD treatment augmented with low intensity care management, feedback to the primary care provider, and training of the clinic providers in management of PTSD.	NR	PCL Mean (SD) G1 Pre-tx: 58.00 (9.95) G1 Post-tx (6 weeks, end of treatment): 50.72 (18.76) G1 Post-tx (12 weeks post randomization): 43.80 (18.33) G1 Post-tx (18 weeks post randomization): 44.58 (16.43) G2 Pre-tx: 54.48 (11.23) G2 Post-tx (6 weeks, end of treatment): 48.52 (13.97) G2 Post-tx (12 weeks post randomization): 47.36 (17.45) G2 Post-tx (18 weeks post randomization): 42.74 (14.42) Treatment by time interaction, F(3, 186) = 3.72, p = 0.12 Largest treatment effect seen at 12 weeks post randomization (6 week followup), t(186)=2.44, p=.016 and diminishing by the 18-week post randomization (12 week followup) assessment (presented in figure) Effect Sizes 6-week (end of treatment): 0.23 12-week (6 weeks posttreatment): 0.47 18-week (12 weeks posttreatment): 0.08	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Fecteau et al., 1999[38]	G1: CBT-mixed (Coping skills, exposure-therapy, and cognitive restructuring) G2: WL	CAPS-2 Mean (SD) G1 Pre-tx: 70.9 (16.2) G1 Post-tx: 37.5 (30.4) G2 Pre-tx: 77.3 (22.7) G2 Post-tx: 74.6 (24.7) Group effects, p<0.01	IES-I Mean (SD) G1 Pre-tx: 20.4 (8.7) G1 Post-tx: 8.3 (8.9) G2 Pre-tx: 24.8 (8.0) G2 Post-tx: 24.4 (8.4) Group Effects, p<0.01 IES-A Mean (SD) G1 Pre-tx: 24.7 (8.2) G1 Post-tx: 7.2 (11.4) G2 Pre-tx: 26.5 (10.5) G2 Post-tx: 24.4 (6.3) Group Effects, p<0.001 Followup for G1 Only IES Mean (SD) G1 Pre-tx: 46.1 (14.7) G1 Post-tx: 15.5 (19.6) G1 3 mth FU: 13.0 (14.9) G1 6 mth FU: 8.3 (7.0) 3 mth change, p<0.001 (n = 10) 6 mth change, p<0.001 (n = 8)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Foa et al., 1999[14] Zoellner et al., 1999[134]	G1: CBT, exposure-based therapy (PE) G2: CBT, coping skills therapy SIT G3: CBT-mixed Combined treatment (PE and SIT) G4: WL	PSS-I Mean (SD) G1 Pre-tx: 29.48 (9.94) G1 Post-tx: 11.70 (7.32) G1 3 mth FU: 11.84 (9.01) G1 6 mth FU: 11.16 (7.38) G1 12 mth FU: 10.69 (8.96) G2 Pre-tx: 29.42 (8.69) G2 Post-tx: 12.89 (8.96) G2 3 mth FU: 15.06 (13.33) G2 6 mth FU: 11.24 (11.86) G2 12 mth FU: 12.64 (14.71) G3 Pre-tx: 29.95 (6.97) G3 Post-tx: 13.55 (9.35) G3 3 mth FU:11.45 (9.03) G3 6 mth FU: 13.17 (10.98) G3 12 mth FU: 12.56 (12.25) G4 Pre-tx 32.93 (5.89) G4 Post-tx: 26.93 (8.47) Main Effects, p<0.01 G1 vs. G4, p<0.001 G2 vs. G4, p<0.05 G3 vs. G4, p<0.05 G1 vs. G2, p=0.14 G1 vs. G3, p=0.11	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Foa et al., 2005[12]	G1: CBT, exposure-based therapy(PE) G2: CBT-mixed (PE plus CR) G3: WL	PSS-I Mean (SD) G1 Pre-tx: 34.0 (5.9) G1 Post-tx: 17.9 (14.5) G2 Pre-tx: 31.1 (8.1) G2 Post-tx: 16.8 (13.2) G3 Pre-tx: 33.3 (6.2) G3 Post-tx: 26.8 (9.6) Group X Time interaction, p<0.01 G1 vs. G3 t-test, p<0.001	NR	NR NR
Fonzo et al., 2017[137] Fonzo et al., 2017[21]	G1: PE G2: WL	CAPS Mean (SD) G1 Pre-tx: 66.33 (15.17) G1 Post-tx: 29.60 (21.26) G2 Pre-tx: 71.37 (14.99) G2 Post-tx: 64.23 (21.77) Group X Time interaction, p<0.001	PTSD Checklist for DSM-IV-Civilian Version Mean (SD) G1 Pre-tx: 56.16 (10.61) G1 Post-tx: 26.13 (7.08) G2 Pre-tx: 57.36 (12.04) G2 Post-tx: 49.00 (13.35) Group X Time interaction, p<0.001	Remission (CAPS ≤20) G1:10 G2:0 Loss of PTSD Diagnosis G1: 21 G2: 0
Forbes et al., 2012[4]	G1: CBT, cognitive processing therapy G2: TAU	CAPS Mean (SD) G1 Pre-tx: 75.53 (16.35) G1 Post-tx: 48.03 (27.89) G1 3 month FU: 45.30 (28.15) G2 Pre-tx: 64.55 (19.46) G2 Post-tx: 57.73 (20.01) G2 3 month FU: 52.55 (18.93) Change over time Post-tx, p=0.002 Post vs. 3 month FU, p=0.649	PCL Mean (SD) G1 Pre-tx: 61.63 (11.50) G1 Post-tx: 45.67 (16.66) G1 FU: 41.13 (17.51) G2 Pre-tx: 57.45 (12.55) G2 Post-tx:53.84 (11.11) G2 FU: 49.11 (11.00) Change over time Post-tx, p=0.007 FU, p=0.943	Loss of PTSD diagnosis G1:30 G2: 10

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ford et al., 2011[59]	G1: TARGET G2: PCT G3: WL	CAPS Mean (SD) G1 Pre-tx: 62.3 (18.1) G1 Post-tx:38.7 (25.6) G2 Pre-tx: 61.9 (21.3) G2 Post-tx: 39.7 (21.4) G3 Pre-tx: 68.7 (17.0) G3 Post-tx: 62.5 (23.3) Group X Time Effect, p<0.001	NR	Met Criteria for full remission at Posttreatment G1: 21% G2: 15% G3: 0 G1 vs. G2, p=0.45 G1 vs, G3, p<0.001 G2 vs. G3, p=0.007 Met Criteria for full remission at 3 month FU G1:29% G2:19% Met Criteria for full remission at 6 month FU G1: 33% G2: 24.5% Approximately 60% in each group were in partial remission. Lost of PTSD diagnosis Baseline to Post-tx G1:35% G2: 29% G3: 11%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ford et al., 20131[60]	G1: TARGET G2: SGT	CAPS Mean (SD) G1 Pre-tx: 65.3 (18.0) G1 Post-tx: 50.0 (20.8) G2 Pre-tx: 63.1 (21.7) G2 Post-tx: 50.5 (24.3) Treatment X Time Interaction at post-tx, F= 0.3, NS, d = 0.13	NR	Full remission (no full PTSD or partial PTSD at post-tx) G1: 4 (12%) G2: 8 (23%) Loss of PTSD Diagnosis (no longer meet criteria for full PTSD at post-tx) G1: 17 (43%) G2: 15 (44%)
Friedman et al., 2007[70]	G1: Sertraline 25 to 200 mg/day G2: Placebo	CAPS-2 Change at Endpoint (SE) G1: -13.1(3.0) G2: -15.4(3.1) Between Group Differences, NS	IES Change at Endpoint (SE) G1: -8.7(1.8) G2: -8.1(1.9) Between Group Differences, NS DTS Change at Endpoint (SE) G1: -11.4 (3.5) G2: -10.5 (3.5) Between Group Differences, NS MISS-Civilian Trauma Version Change at Endpoint (SE) G1: -4.3 (1.7) G2: -2.8 (1.7) Between Group Differences, NS	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Galovski et al., 2012[6]	G1: Modified CBT. Modifications include potential addition of stressor sessions and variable length of treatment. G2: Delayed treatment symptom monitoring	CAPS LSM (SE) G1 Pre-tx: 74.45 (2.42) G1 Post-tx: 26.96 (3.88) Difference: -47.5 G2 Pre-tx: 77 (2.57) G2 Post-tx: 61.18 (3.98) Difference: -15.8 (Hedge's g = 1.35) G1 vs. G2 Difference, -31.7, p <0.001	PDS LSM (SD) G1 Pre-tx: 31.88 (1.25) G1 Post-tx: 11.63 (2.01) Difference: -20.3 G2 Pre-tx: 35.28 (1.24) G2 Post-tx: 26.81 (2.07) Difference: -8.5 (Hedge's g = .86) G1 vs. G2 Difference,-12.7, p <0.001	NR NR
Gamito et al., 2010[141]	G1: VRET G2: CBT, exposure-based therapy (Imaginal exposure) G3: WL	CAPS G1 Percentage variation: -8 G2 Percentage variation: -1 G3 Percentage variation: -6 Effects, NS	IES-R G1 Percentage variation: -1 G2 Percentage variation: 1 G3 Percentage variation: 7	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Gersons et al., 2000[51]	G1: Eclectic psychotherapy (Brief Eclectic Psychotherapy) G2: WL	NR	NR	Proportions by Treatment (%, p values) No PTSD Posttest G1: 91% G2: 50% p<0.01 3-month Followup G1: 96% G2: 35% p<0.01 NR
Haller et al., 2016[145]	G1: Group ICBT for depression and SUD plus CPT-M (trauma-focused CPT modified to include substance use prevention) (individual) G2: Group ICBT for depression and SUD plus ICBT for depression and SUD (individual)	NR	PCL Mean (SD) G1 Pre-tx: 51.46 (15.48) G1 Post-tx: 49.62 (14.04) G1 Post-tx (1 year followup): 48.33 (17.14) G2 Pre-tx: 49.88 (16.06) G2 Post-tx: 46.69 (15.74) G2 Post-tx (1 year followup): 39.47 (16.46) Scores were lower at the one year followup for participants in G2 compared to G1, F(1,71)= 5.58, p =.023. (based on only those participants who were assessed) Trajectory models that account for missing values did not indicate significant differences between groups over time.	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Hamner et al., 2003[83]	G1: Risperidone 1 to 6 mg/day G2: Placebo	CAPS Mean (SD) G1 Pre-tx: 90.3 (23.0) G1 Post-tx: 81.3 (24.3) G2 Pre-tx: 89.1 (12.2) G2 Post-tx: 79.0 (21.0) Between-treatment changes, NS	NR	NR NR
Harned et al., 2014[144]	G1: DBT plus DBT PE G2: DBT	PSS-I Mean (SD) G1 Pre-tx: 32.8 (8.0) G1 Post-tx: 13.6 (13.2) G1 3 month followup: 16.7 (14.1) G2 Pre-tx: 30.1 (9.6) G2 Post-tx: 13.8 (9.3) G2 3 month followup: 18.4 (7.7) Between Group Effect size, Post: 0.0, followup: 0.1 Treatment X time Interaction, F = 0.3 (3, 42), NS	NR	Loss of Diagnosis: Post-tx (ITT) (Defined as no longer meeting DSM-IV criteria for PTSD) G1: 58.3% G2:33.3% Remission at 3 month followup G1: 50% G2: 0

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Hien et al., 2004[57]	G1: Seeking Safety G2: Relapse prevention condition (only substance abuse) G3: UC (Non-randomized Standard community Care)	CAPS Frequency and Intensity Mean (SD) G1 Pre-tx: 72.17 (19.70) G1 Post-tx: 57.15 (22.33) G1 6 mth FU: 59.85 (21.12) G1 9 mth FU: 55.34 (20.85) G2 Pre-tx: 70.38 (16.84) G2 Post-tx: 51.21 (25.21) G2 6 mth FU: 52.65 (24.08) G2 9 mth FU: 47.82 (27.73) G3 Pre-tx: 73.88 (19.16) G3 Post-tx:68.00 (24.20) G3 6 mth FU:64.79 (23.81) G3 9 mth FU: 66.00 (23.99) CAPS Global Severity Mean (SD) G1 Pre-tx: 2.73 (0.63) G1 Post-tx: 2.14 (1.53) G1 6 mth FU: G1 9 mth FU: 1.79 (0.63) G2 Pre-tx: 2.41 (0.70) G2 Post-tx:1.75 (0.79) G2 6 mth FU: 1.62 (0.65) G2 9 mth FU: 1.40 (1.12) G3 Pre-tx: 2.82 (1.16) G3 Post-tx: 2.43 (1.09) G3 6 mth FU: 2.35 (0.70) G3 9 mth FU: 2.14 (1.07) Significance NR for CAPS	IES-R Mean (SD) G1 Pre-tx: 47.49 (14.50) G1 Post-tx: 33.57 (14.92) G1 6 mth FU: 39.12 (17.23) G1 9 mth FU: 35.11 (16.82) G2 Pre-tx: 46.12 (10.57) G2 Post-tx: 28.90 (19.94) G2 6 mth FU: 36.38 (20.16) G2 9 mth FU: 29.67 (18.84) G3 Pre-tx: 51.52 (12.76) G3 Post-tx: 40.64 (20.43) G3 6 mth FU: 40.06 (17.62) G3 9 mth FU: 47.57 (13.21)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Hien et al., 2009[157] Hien et al., 2012[158]	G1: Seeking Safety G2: Psychoeducation	CAPS, ITT Analysis Data Mean (SD) G1 Pre-tx: 61.6 (19.4) G1 Post-tx: 31.7 (23.4) G1 Average of FU: 24.3 (22.1) G2 Pre-tx: 64.2 (19.4) G2 Post-tx.: 32.7 (23.4) G2 Average of FU: 27.1 (23.4) Post-tx G1 vs. G2, p<0.001	PSS-SR, ITT Analysis Data Mean (SD) G1 Pre-tx: 45.4 (15.3) G1 Post-tx: 32.7 (13.9) G1 Average Over FU: 30.0 (13.0) G2 Pre-tx: 45.6 (15.3) G2 Post-tx.: 33.8 (15.1) G2 Average Over FU: 32.0 (15.0) Post-tx G1 vs. G2, p=0.59 12-mth FU (Average Over) G1 vs. G2, p=0.97	NR NR
Hinton et al., 2005[34]	G1: CBT-mixed (Information on PTSD and Panic Disorder, relaxation techniques, culturally appropriate visualization, cognitive restructuring, exposure to anxiety-related sensations and trauma related memories, emotional-processing protocol, and cognitive flexibility) G2: WL	CAPS Mean (SD) G1 Pre-tx: 74.85 (14.67) G1 2nd Assessment: 39.25 (19.92) G1 3rd Assessment: 41.30 (13.95) G1 FU Assessment: 44.56 (14.58) G2 Pre-tx: 75.91 (11.5) G2 2nd Assessment: 73.05 99.43) G2 3rd Assessment: 45.05 (8.72) G2 FU Assessment: 43.56 (10.22) Group Diffferences at 2nd Assessment, p<0.001 Group Differences at 1st, 3rd, & 4th assessments, NS	NR	NR Percentage who no longer met PTSD criteria at assessment 2 G1: 60% (n= 12) G2: 0% p<0.001

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Hinton et al., 2009[151]	G1: CBT-Mixed (Information on PTSD and Panic Disorder, muscle relaxation, guided imagery, mindfulness training, yoga-like stretching, cognitive restructuring, various exercises to teach emotional distancing and switching, and interoceptive exposure) G2: WL	CAPS Mean (SD) G1 Pre-tx: 75.41 (13.47) G1 2nd Assessment: 46.83 (17.17) G1 3rd Assessment: 44.75 (14.85) G2 Pre-tx: 77.25 (11.47) G2 2nd Assessment: 74.25 (9.43) G2 3rd Assessment: 45.83 (8.45) Between group difference at 2nd assessment, p<0.01 Between group differences at 3rd assessment, NS	NR	NR NR
Hinton et al., 2011[152]	G1; CBT-mixed Culturally Adapted CBT (coping skills, cognitive "modification", mentions exposure) G2: Applied Muscle Relaxation	NR	PTSD Checklist Mean (SD) G1 Pre-tx: 69.8 (6.5) G1 Post-tx: 39.1 (15.1) G1 FU: 36.4 (12.7) G2 Pre-tx: 71.1 (7.9) G2 Post-tx: 61.6 (13.2) G2 FU: 58.9 (14.7) Post-tx G1 vs. G2, p<0.05 (t-test) FU G1 vs. G2, p<0.05 (t-test)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Hogberg et al., 2007[48]	G1; EMDR G2: WL	NR	IES Mean (SD) Pre-tx G1 Pre-tx: 39.3 (17.2) G1 Post-tx: 23.2 (17.4) G2 Pre-tx: 39.1 (12.6) G2 Post-tx: 34 (16.2) Within-group effect over time: G1: p<0.05 G2: p<0.05 Between group differences, NS	NR 6 EMDR patients retained PTSD diagnosis, but denominator not given G1:67% (8 of 12) G2: 11% (1 of 11) p=0.02
Hollifield et al., 2007[32]	G1: Acupuncture G2: CBT-mixed (Cognitive restructuring, behavior activation, and coping skills) G3: WL	NR	PSS-SR Mean (SD) G1 Pre-tx: 31.33 (10.10) G1 Post-tx: 15.65 (13.95) G1 3 mth FU: 15.42 (12.54) G2 Pre-tx: 32.52 (6.63) G2 Post-tx: 20.02 (10.56) G2 3 mth FU: 16.68 (12.20) G3 Pre-tx: 30.79 (9.54) G3 Post-tx: 27.92 (12.33) G3 3 mth FU: 27.92 (12.33) RMANOVA G1 vs. G2, p=0.29 G1 vs. G3, p<0.01 G2 vs. G3, p<0.01	NR PSS-SR <16 at end of tx: G1: 68% G2: 43% G3: 19% PSS-SR <16 at 3-months: G1: 68% G2: 62%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ivarsson et al., 2014[24]	G1: Internet based CBT G2: Delayed treatment attention control	NR	IES - (ITT) Mean (SD) G1 Pre-tx: 54.65 (13.16) G1 Post-tx: 30.96 (16.06) G2 Pre-tx: 54.87 (15.48) G2 Post-tx:49.19 (18.09) Differential average rates of changes between pre-and post treatment as a function of condition, -17.9 (95% CI, -25.2 to -10.6), t (58) = 4.9, P<0.001, d = 1.25 (95% CI, 0.65 to 1.80), favoring treatment PDS - (ITT) Mean (SD) G1 Pre-tx: 31.90 (6.52) G1 Post-tx: 17.32 (9.86) G2 Pre-tx: 29.84 (8.77) G2 Post-tx:25.04 (11.14) Treatment by time interaction =, -9.6 (95% CI, -13.8 to -5.3), t (54) = 4.5, P<0.001, d = 1.24 (95% CI, 0.64 to 1.81), favoring treatment	Remission: NR Loss of Diagnosis (no longer met criteria for PTSD based on CAPS): G1:81.5% (22) G2: 38.9 (14) Est = -1.55, SE = 0.62, p = 0.01, OR = 0.12, (95% CI, 0.06 to 0.71) Improvement based on CGI G1:63% (17) G2:13.8% (4) Est = 2.36, SE = 0.67, p = 0.001, OR = 10.63, (95% CI, 2.86 to 39.5)
Johnson et al., 2011[29]	G1: CBT-mixed (Psychoeducation and CBT restructuring) G2: UC	CAPS Mean (SD) G1 Pre-tx: 53.34 (24.29) G1 Post-tx: 24.76 (18.47) G1 3 mth FU: 21.15 (24.79) G1 6 mth FU: 18.62 (18.84) G2 Pre-tx: 62.69 (25.38) G2 Post-tx: 42.38 (29.33) G2 3 mth FU: 31.27 (22.01) G2 6 mth FU: 26.56 (25.83) Time effect, *p*<0 .0001 Treatment effect, p>0.05	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Kearney et al., 2013[159]	G1: MBSR+TAU G2: TAU (VHA health system)	NA	PCL Mean (SD) G1 Pre-tx: 59.88 (11) G1 Post-tx: 52.45 (13) G1 4 month followup: 54.43 (15) G2 Pre-tx: 62.91 (11) G2 Post-tx: 58.5 (11) G2 4 Month followup: 60.16 (13) Post-tx, Between group: d = -.51 (95%, CI, -1.12 to 0.11) 4 month followup: d = -.42 (95%, CI, -1.03 to 0.2) Clinically meaningful change (>=10 points) at PostTx: Mindfulness: 8 (36.4%) TAU: 5 (25%) Clinically meaningful change (>=10 points) at 4months: Mindfulness: 9 (39.1%) TAU: 5 (26.3%)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Krakow et al., 2001[52]	G1: IRT G2: WL	CAPS Mean (SD) G1 Pre-tx: 81.88 (16.96) G1 Post-tx: 49.58 (23.96) Change: 32.3 (21.40) G1 Pre-tx: 79.62 (24.37) G2 Post-tx: 68.37 (27.26) Change: 11.25 (21.65) G1 vs. G2, p<0.001 PSS Mean (SD) G1 Pre-tx: 28.29 (10.37) G1 Post-tx: 17.19 (10.39) Change: 11.1 (11.06) G1 Pre-tx: 28.48 (11.73) G2 Post-tx: 25.26 (11.78) Change: 3.22 (9.02) G1 vs. G2, p<0.001	NR	NR NR
Krystal et al., 2011[85]	G1; Risperidone 1 to 4 mg/day G2: Placebo	CAPS Mean Difference (95 % CI) 2.73 (-0.74 to 6.20) p=0.12	NR	% of veterans remitted based on CAPS at 24 weeks ǂ G1: 4.9 G2: 4.0 % of veterans with mild symptoms/ subdiagnostic based on CAPS at 24 weeks ǂ G1: 14.6 G2: 6.5

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Kubany et al., 2003[35]	G1: CBT, cognitive restructuring G2: WL	CAPS Mean (SD) G1 Pre-tx: 80.9 (20.7) G1 Post-tx: 10.1 (19.3) G1 3 mth FU: 7.9 (9.3) G2 Pre-tx: 79.1 (22.1) G2 Post-tx: 76.1 (25.2) G2 Post-therapy: 11.6 (13.6) G2 3 mth FU: 12.4 (13.8) G1 Post-tx change, p<0.05 G2 Post-tx change, NS G1 3 mth change, NS G2 Post-therapy, p<0.05 G2 3 mth change, NS	NR	NR No longer met diagnostic criteria for PTSD Based on CAPS G1: 94.0% G1: 0.0%
Kubany et al., 2004[28]	G1: CBT-Mixed (Cognitive Trauma Therapy-Battered Women) G2: WL	CAPS (ITT Sample) Mean (SD) G1 Pre-tx:74.4 (19.9) G1 Post-tx: 33.3 (32.8) G2 Pre-tx: 78.0 (20.5) G2 Post-tx: 74.1 (21.9) Between group significance, NR	NR	NR Lost of PTSD diagnosis based on completers G1: 91% G2: NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Langkaas et al., 2017[142]	G1: PE G2: IRT	PSS-I Mean (SD) G1 Pre-tx: 34.9 (8.25) G1 Post-tx: 19.7 (13.92) G1 3 mth FU: 22.9 (15.74) G2 Pre-tx: 33.2 (6.91) G2 Post-tx: 21.9 (14.13) G2 12 mth FU: 23.5 (15.13) Treatment X Time Interaction, NS	NR	Recovered G1 Post-tx: 48% G2 Post-tx: 50% G1 12 mth FU:39% G2 12 mth FU:38% Improved G1 Post-tx: 13% G2 Post-tx: 6% G1 12 mth FU:13% G2 12 mth FU: 9% Loss of Diagnosis NR
Li et al., 2017[172]	G1; Sertraline 135 mg G2: Placebo	NR	IES-R Change at endpoint G1: -24.3 (-32.1 to -14.3) G2:-18.1 (-25.7 to -11.8) Difference between groups: -6.4 to -2.6), p <0.01	CGI-Severity Change at endpoint G1: -1.0 (-1.6 to -0.4) G2:-0.6 (-1.3 to -0.2) Difference between groups: -0.4 to -0.2), p <0.01 Symptom reduction G1: 36 (100%) G2:25 (75%) Loss of PTSD diagnosis NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Lindauer et al., 2005[50]	G1: Eclectic psychotherapy Brief Eclectic Psychotherapy G2: WL	SI-PTSD Reexperiencing Score Mean (SD) G1 Pre-tx: 3.4 (0.9) G1 Post-tx: 1.2 (1.5) G2 Pre-tx: 3.9 (0.8) G2 Post-tx: 3.1 (1.8) G1 vs. G2, p<0.05 SI-PTSD Avoidance Score Mean (SD) G1 Pre-tx: 3.9 (1.1.) G1 Post-tx: 1.6 (2.2) G2 Pre-tx: 3.5 (0.7) G2 Post-tx: 3.2 (1.7) G1 vs. G2, NS SI-PTSD Hyperarousal Mean (SD) G1 Pre-tx: 3.8 (0.9) G2 Post-tx: 1.3 (1.8) G2 Pre-tx: 3.8 (1.0) G2 Post-tx: 2.7 (1.5) G1 vs. G2, p<0.05	NR	NR SI-PTSD scale used to diagnose PTSD, % improved at Post-tx G1: 83.3% G2: 25% p<0.05

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Litz et al., 2007[33]	G1: CBT-mixed (Stress management skills, in vivo exposure, and relapse prevention) G2: Internet-delivered supportive counseling	PSS-I Mean (SD) (Completer Group) G1 Pre-tx: 26.71 (9.02) G1 Post-tx: 14.86 (13.35) G1 3 mth FU: 13.20 (8.63) G1 6 mth FU: 8.67 (7.98) G2 Pre-tx: 29.16 (9.93) G2 Post-tx: 20.00 (11.50) G2 3 mth FU: 13.96 (8.63) G2 6 mth FU: 17.50 (10.40) ITT Analysis Post-tx Time effect, p<0.001 3 mth FU G1 v.s G2, NS Completer Analysis 3 mth FU G1 vs. G2, NS 6 mth FU Group Effect, p =0.06		NR % no longer meeting criteria for PTSD based on PSS-I <6 ITT Analysis Post-tx: G1:25% G2: 5% Likelihood ratio=3.89, p<0.05 3-mth F/U, p=NR 6 mth F/U G1: 25% G2: 3% Likelihood ratio=8.35, p<0.01
Maguen et al., 2017[25]	G1: CBT, Impact of Killing (IOK) G2: WL	NR	PCL Mean (SD) G1 Pre-tx: 48.6 (14.5) G1 Post-tx: 41.3 (11.2) Mean change: -7.33 (-14.71 to -0.05), t-test p = 0.0512 G2 Pre-tx: 52.9 (11.3) G2 Post-tx: 50.7 (10.6) Mean change: -2.13 (-5.97 to -1.71), t-test p = 0.2534 Between-group difference: -7.27 (-13.89 to -0.64), t-test p=0.033	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Markowitz et al., 2015[132] Markowitz et al., 2016[261]	G1: PE G2: IPT G3: RT	CAPS Mean (SD) G1 Pre-tx: 72.1 (18.2) G1 Post-tx: 37.5 (28.8) Change at Post-tx: 31.6, Effect size: 1.88 G2 Pre-tx: 68.9 (16.2) G2 Post-tx: 39.8 (24.3) Change at Post-tx: 28.6, Effect size: 1.69 G3 Pre-tx: 68.9 (16.4) G3 Post-tx: 46.5 (31.0) Change at Post-tx: 22.3, Effect size: 1.32 Treatment X Time Interaction at post-tx, X^2= 1.07, p = 0.343 G1 vs. G3 Difference: -14.93, p = 0.010, Effect Size: -0.88 G2 vs. G3 Difference: -9.47, p = 0.097, Effect Size: -0.56 G2 vs. G1 Difference: 5.46, p = 0.323, Effect Size: 0.32	Post Stress Scale Mean (SD) G1 Pre-tx: 77.7 (22.3) G1 Post-tx: 34.1 (26.4) Change at Post-tx: 36.1, Effect size: 1.81 G2 Pre-tx: 74.3 (20.2) G2 Post-tx: 41.7 (26.1) Change at Post-tx: 32.1, Effect size: 1.61 G3 Pre-tx: 83.2 (15.3) G3 Post-tx: 64.7 (27.4) Change at Post-tx: 14.1, Effect size: 0.71 Treatment X Time Interaction at post-tx, X2= 4.67, p = 0.010 G1 vs. G3 Difference: -30.75, p < 0.001, Effect Size: -1.55 G2 vs. G3 Difference: -18.22, p = 0.008, Effect Size: -0.92 G2 vs. G1 Difference: 12.54, p = 0.053, Effect Size: 0.63	Remission (CAPS score <20) G1: 26% G2: 23% G3: 22 % NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Marks et al., 1998[122] Lovell et al., 2001[123]	G1: CBT, exposure-based therapy(PE) G2: CBT, cognitive restructuring G3: CBT-mixed Exposure (Combined with CR) G4: Relaxation	Marks et al., 1998[122] CAPS-2, Mean Change Score at Post-tx (95% CI) G1: 30 (19 to 42) G2: 36 (26 to 45) G3: 38 (26 to 50) G4: 14 (4 to 25) Additional results presented in graphs CAPS Mean change in G1 + G2 + G3 vs. G4 Post, p=0.005 1 mth FU, p=0.01 3 mth FU, p=0.005 Lovell et al., 2001[123] CAPS, Re-experiencing subscale Mean (SD) G1 Pre-tx: 13.3 (3.9) G1 Post-tx: 6.8 (7.5) G2 Pre-tx: 14.9 (5.0) G2 Post-tx: 7.8 (4.9) G3 Pre-tx: 15.1 (6.4) G3 Post-tx: 6.8 (7.2) G4 Pre-tx: 11.6 (6.1) G4 Post-tx: 9.7 (7.4) Post-tx G1 + G2 +G3 vs. G4, p<0.02 Followups G1 + G2 +G3 vs. G4, NS	IES (first 11 weeks) Mean Change Score (95% CI) G1: 28 (19 to 37) G2: 25 (15 to 34) G3: 35 (24 to 49) G4: 13 (5 to 19) Additional results presented in graphs IES Mean change in G1 + G2 + G3 vs. G4 Post, p=0.008 1 mth FU, p=0.08 3 mth FU, p=0.05	NR PTSD Criteria not meet by CAPS G1: 75% G2: 65% G3: 63% G4: 55%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Marks et al., 1998[122] Lovell et al., 2001[123]cont'd		CAPS, Advoidance/numbing subscale Mean (SD) G1 Pre-tx: 23.4 (8.3) G1 Post-tx: 11.5 (13.1) G2 Pre-tx: 30.7 (7.6) G2 Post-tx: 15.2 (11.0) G3 Pre-tx: 29.8 (9.3) G3 Post-tx: 11.9 (11.9) G4 Pre-tx: 23.0 (9.1) G4 Post-tx: 17.1 (8.9) Post-tx G1 + G2 +G3 vs. G4, p<0.004 1 month FU G1 + G2 +G3 vs. G4, p<0.02 3 month FU G1 + G2 +G3 vs. G4, p<0.01 CAPS, Increased arousal subscale Mean (SD) G1 Pre-tx: 25.2 (8.5) G1 Post-tx: 13.2 (11.1) G2 Pre-tx: 29.1 (8.8) G2 Post-tx: 16.5 (10.0) G3 Pre-tx: 28.6 (7.7) G3 Post-tx: 16.6 (11.7)		

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Marks et al., 1998[122] Lovell et al., 2001[123]cont'd		G4 Pre-tx: 23.7 (7.6) G4 Post-tx: 17.0 (10.5) Post-tx G1 + G2 +G3 vs. G4, NS		
Marks et al., 1998[122] Lovell et al., 2001[123]cont'd		Followups G1 + G2 +G3 vs. G4, NS CAPS, Associated features subscale Mean (SD) G1 Pre-tx: 16.7 (9.0) G1 Post-tx: 8.1 (9.7) G2 Pre-tx: 22.6 (10.2) G2 Post-tx: 10.3 (8.8) G3 Pre-tx: 20.8 (10.8) G3 Post-tx: 11.0 (11.0) G4 Pre-tx: 15.2 (8.0) G4 Post-tx: 12.0 (11.0) Post-tx G1 + G2 +G3 vs. G4, p<0.04 Followups G1 + G2 +G3 vs. G4, NS		

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Marshall et al., 2001[64]	G1: Paroxetine 20 mg/day G2: Paroxetine 40 mg/day G3: Placebo	CAPS-2 Adjusted Mean Differences (95% CI) G1 vs. G3 -14.3 (-19.7 to -8.8) p<0.001 G2 vs. G3 -12.2 (-17.7 to -6.6) p<0.001 TOP-8 Adjusted Mean Differences (95% CI) G1 vs. G3 -3.4 (-5.1 to -1.8) p<0.001 G2 vs. G3 -2.9 (-4.5 to -1.3) p<0.001	DTS Adjusted Mean Differences (95% CI) G1 vs. G3 -12.2 (-18.1 to -6.3) p<0.001 G2 vs. G3 -10.9 (-16.9 to -4.9) p<0.001	NR NR
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	G1: Fluoxetine 20 to 80 mg/day G2: Placebo	CAPS Changes from Pre-tx to Post-tx Least Square Means (SD), p-value G1: -34.6 (28.1) G2: -26.8 (26.1) p=0.021 TOP-8 Changes from Pre-tx to Post-tx Least Square Means, p-value G1: -10.3 G2: -8.0 p=0.006	DTS Changes from Pre-tx to Post-tx Least Square Means (SE), p-value G1: -33.8 (2.25) G2: -27.3 (3.66) p=0.117	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Martenyi et al., 2007[62]	G1: Fluoxetine 20 mg/day G2: Fluoxetine 40 mg/day G3: Placebo	CAPS Mean change from baseline (SD) ITT Analysis G1: -42.9 (23.1) G2: -42.8 (27.9) G3: -36.6 (25.7) Overall p-value= 0.15 TOP-8 Mean change from baseline (SE) Completer analysis G1: -10.59 (0.58) G2: -10.25 (0.60) G3: -10.59 (0.81) Overall p-value= 0.907	NR	NR Loss of PTSD Diagnosis G1: 40.5% G2: 38.8% G3: 37.5
Maxwell et al., 2016[124]	G1: MEST G2: CPT	NR	MPSS-SR Mean (SD) G1 Pre-tx:63.50 (18.37) G1 Post-tx:54.13 (24.87) G1 3 mth FU: 33.5 (25.39) G2 Pre-tx:49.00 (26.60) G2 Post-tx:38.13 (15.06) G2 3 mth FU: 25.13 (23.31) Cohen's d = .50	NR NR
McDonagh et al., 2005[39]	G1: CBT-mixed (Exposure and cognitive restructuring therapy) G2: PCT G3: WL	CAPS Mean (SD) G1 Pre-tx: 69.9 (16.8) G1 Post-tx: 53.1 (28.8) G2 Pre-tx: 67.7 (14.6) G2 Post-tx: 47.2 (22.4) G3 Pre-tx: 72.0 (17.6) G3 Post-tx: 65.5 (18.6) Group X Time, p<0.10	NR	NR No longer met criteria for PTSD (CAPS) G1: 27.6% G2: 31.8% G3: 17.4%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
McGovern et al., 2015[27]	G1: ICBT plus SC, manual-guided therapy focused on PTSD and substance use. G2: IAC plus SC, (focused exclusively on substance use and recovery) (arm not eligible) G3: SC (intensive out-patient program services)	CAPS Mean (SD) G1 Pre-tx: 76.71 (18.13) G1 Post-tx (6 month): 46.81(24.81) G3 Pre-tx: 76.51 (20.83) G3 Post-tx (6 month):52.60(26.46) NS difference between G1 and G3 Parameter Estimate and CIs G1 vs. G3, -4.95 (95% CI, -13.65 to 3.74) Effect size G1 vs. G3: -0.24	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Mills et al., 2012[20]	G1: COPE, a modification of Concurrent Treatment of PTSD and Cocaine Dependence. (motivational enhancement, psychoeducation, in vivo exposure, imaginal exposure, and cognitive therapy) G2: TAU.	CAPS Mean (95% CI) G1 Pre-tx: 91.13 (87.03 to, 95.23) G1 Post-tx: 52.90 (43.72 to 62.06) Mean difference: -38.24 (-47.93, -28.54), p < 0.001 G2 Pre-tx: 89.83 (84.70 to 94.06) G2 Post-tx: 67.23 (59.21 to 75.25) Mean difference: -22.14 (-30.33 to -13.95), p < 0.001 Between group difference Pre-tx to FU: -16.09 (-29.00 to -3.19), p = 0.02 Treatment X Time Interaction: $X^2 = 5.38$, p = 0.02	NR	NR NR
Monnelly et al., 2003[167]	G1: Risperidone 0.5 to 2.0mg/day G2: Placebo	NR	PCL-M Median Change Scores G1: -10.0 G2: -0.5 p=0.02	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Monson et al., 2006[1]	G1: CBT, CPT G2: WL	CAPS Mean (SE) G1 Pre-tx: 76.73 (2.6) G1 Post-tx: 52.14 (3.9) G1 1 mth FU: 58.13 (4.5) G2 Pre-tx: 79.10 (3.5) G2 Post-tx: 76.03 (3.7) G1 1 mth FU: 74.37 (4.3) Group X Time, p<0.01	NR	NR Did Not Meet Diagnostic Criteria for PTSD at Post-treatment G1: 40% (n=12) G2: 3% (n=1) p<0.001 Did Not Meet Diagnostic Criteria for PTSD at 1-month G1: 30% (n= 9) G2: 3% (n=1) p=0.01
Monson et al., 2012[22]	G1: CBCT, manualized cognitive-behavioral conjoint therapy for PTSD delivered in a couple therapy format G2: WL	CAPS Mean (95% CI) G1 Pre-tx: 68.87 (62.12 to 75.61) G1 Post-tx: 33.45 (22.03 to 44.87) Change: -35.42 (-47.84 to -23.00) Effect size Hedge g: 1.82 (1.00 to 2.62) G2 Pre-tx: 73.03 (66.29 to 79.76) G2 Post-tx: 60.82 (49.87 to 71.78) Change: -12.20 (-21.51 to -2.89) Effect size Hedge g: 0.57 (0.12 to 1.00) Change Difference Mean Between Groups: -23.21 (-37.87 to -8.55)	PTSD Checklist Mean (95% CI) G1 Pre-tx: 49.92 (45.12 to 54.71) G1 Post-tx: 30.38 (22.81 to 37.96) Change: -19.53 (-27.30 to -11.77) Effect size Hedge g: 1.61 (0.83 to 2.37) G2 Pre-tx: 57.89 (53.10 to 62.67) G2 Post-tx: 46.80 (36.61 to 53.99) Change: -11.09 (-18.34 to -3.85) Effect size Hedge g: 0.71 (0.21 to 1.20) Change Difference Mean Between Groups: -8.44 (-18.71 to -1.83) Effect size Hedge g: 0.60 (-0.10 to 1.29)	NR Loss of PTSD Diagnosis at posttreatment (not meeting DSM-IV-TR symptom criteria and a total score lower than 45 on the CAPS) G1: 13 (81%) G2: 4 (21%)

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Monson et al., 2012[22] (continued)		Effect size Hedge g: 1.13 (0.40 to 1.85) Treatment X Time Interaction, t (37, 5) = -3.09, p = 0.004		
Moradi et al., 2014[160]	G1: MEmory Specificity Training (MEST) G2: Control, no additional contact	NR	IES-R Treatment X Time Interaction, F(2, 44) = 176.48, p < 0.001, η2 = 0.89	NR NR
Morath et al., 2014[55]	G1: NET G2: WL	CAPS Mean (SD) G1 Pre-tx: 92.41 (14.95) G1 Post-tx: 58.65 (24.93) G1 1 year post-tx:51.88 (24.52) G2 Pre-tx: 76.88 (15.95) G2 Post-tx: 74.59 (20.42) Treatment X Time Interaction at post-tx, F (1, 32) = 16.90, p = 0.0003	NR	NR NR
Mueser et al., 2008[7]	G1: CBT-mixed (CBT for PTSD) G2: UC	CAPS Mean (SD) G1 Pre-tx: 74.46 (17.56) G1 Post-tx: 55.53 (27.92) G1 3 mth FU: 55.10 (25.96) G1 6 mth FU: 57.48 (25.34) G2 Pre-tx: 76.15 (17.07) G2 Post-tx: 67.78 (26.84) G2 3 mth FU: 64.80 (28.25) G2 6 mth FU: 70.90 (24.15) Group effect, p=0.005	NR	NR Loss of PTSD Diagnosis CAPS Dx, n(%) G1 Pre-tx: 54 (100.0) G1 Post-tx: 21 (67.7) G1 3 mth FU: 19 (63.3) G1 6 mth FU: 24 (72.7) G2 Pre-tx: 54 (100.0) G2 Post-tx: 21 (77.8) G2 3 mth: 27 (77.1) G2 6 mth: 17 (85.0) Group effect, p=0.63,

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Nacasch et al., 2011[15]	G1: CBT, exposure-based therapy (Prolonged exposure therapy) G2: TAU	PSS-I Mean (SD) G1 Pre-tx: 37.1 (3.8) G1 Post-tx: 18.9 (9.1) G1 FU: 16.3 (10.4) G2 Pre-tx: 36.8 (6.2) G2 Post-tx: 35.0 (8.9) G2 FU: 35.4 (7.6) Post-tx Treatment X Time, p<0.001 12 month FU Treatment X Time (Pre to FU), p<0.001 Treatment X Time (Post to FU), NS	NR	NR NR
Neuner et al., 2004[161]	G1: CBT, exposure-based therapy (NET) G2: Supportive Counseling G3: Psycho-education About the nature and prevalence of PTSD	Composite International Diagnostic Interview-PTSD Mean (SD) G1 Pre-tx: 13.4 (2.1) G1 1 year FU: 8.9 (2.7) G2 Pre-tx: 13.9 (2.3) G2 1 year FU: 12.6 (3.2) G3 Pre-tx: 14.2 (2.9) G3 1 year FU: 13.4 (3.3) 1 year Group X Time G1 vs. G2, p=0.01 G1 vs. G3, p=0.01	PDS Mean (SD) G1 Pre-tx: 25.2 (7.4) G1 Post-tx: 19.1 (11.7) G1 4 mth FU: 24.5 (7.8) G1 1 year FU: 16.0 (5.1) G2 Pre-tx: 22.0 (8.0) G2 Post-tx:19.8 (10.9) G2 4 mth FU: 22.8 (23.1) G2 1 year FU: 23.1 (7.7) G3 Pre-tx: 19.5 (8.0) G3 Post-tx: 21.2 (9.4) G4 Post-tx: 27.7 (6.6) G3 1 year FU: 23.9 (7.0) 1 year Group X Time G1 vs. G2, p=0.01 G1 vs. G3, p=0.01	NR Percentage of Patients Without a PTSD Diagnosis at 1 year followup G1: 71.0% G2: 21.0% G3: 20.0%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Neuner et al., 2008[54]	G1: CBT, exposure based (NET) G2: Flexible Trauma Counseling G3: No-treatment monitoring group	PDS Mean (SD) G1 Pre-tx: 25.9 (13.2) G1 Post-tx: 5.4 (6.6) G1 6 mth FU: 6.1 (6.8) G2 Pre-tx: 26.7 (12.5) G2 Post-tx: 5.3 (5.7) G2 6 mth FU: 5.0 (6.6) G3 Pre-tx: 21.3 (10.6) G3 Post-tx: NR G3 6 mth FU: 10.1 (8.1) G1 vs. G2 Comparisons Group X Time at Post-tx, p=0.87 Treatment Groups vs. Control Treatment X Time, p=0.01	NR	NR No longer fulfilled criteria for PTSD at 9 months. G1: 69.85% G2: 65.2% G3: 36.8%
Neuner et al., 2010[53]	G1: CBT, exposure based (NET) G2: UC	PDS Mean(SD) G1 Pre-tx: 38.9 (6.4) G1 Post-tx: 26.0 (9.2) G2 Pre-tx: 36.9 (8.0) G2 Post-tx: 34.1 (6.1) Group X Time, p=0.01	NR	NR Loss of PTSD Diagnosis G1: 6.25% G2: 0%
Nijdam et al., 2012[154]	G1: Eclectic psychotherapy G2: EMDR	SI-PTSD Mean Difference at 1st Post (95% CI) 10.80 (6.37 to 15.23) p<0.001 Mean Difference at 2nd Post (95% CI) 2.41 (-2.10 to 6.92) p=0.29	NR	

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Panahi et al., 2011[71]	G1: Sertraline 50 to 200 mg/day G2: Placebo	NR	NR	
Petrakis et al., 2012[185, 240]	G1: Paroxetine (40 mg/day)+ Naltrexone (50 mg/day) Participants who could not tolerate the highest dose were brought to lower doses. G2: Paroxetine (40 mg/day) +Placebo Participants who could not tolerate the highest dose were brought to lower doses. G3: Desipramine (200 mg/day) + Naltrexone (50 mg/day) Participants who could not tolerate the highest dose were brought to lower doses. G4: Desipramine (200 mg/day + Placebo Participants who could not tolerate the highest dose were brought to lower doses.	CAPS Mean(SE) G1 Pre-tx: 73.54 (5.007) G1 Post-tx: 40.024 (5.53) G2 Pre-tx: 69.810 (5.166) G2 Post-tx: 36.591 (5.570) G3 Pre-tx: 62.500 (5.047) G3 Post-tx: 26.751 (5.353) G4 Pre-tx: 77.833 (4.832) G4 Post-tx: 41.392 (4.949) Time effect, p<0.00 Group X Time, NS	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Polusny et al., 2015[136]	G1: 8 weekly group sessions and a daylong retreat. 1st session was an orientation that included rational and psychoeducation. 7 sessions of mindfulness therapy and 1 6.5 hour retreat. G2: Group Sessions	CAPS Mean (95% CI) G1 Pre-tx: 69.9 (51.0 to 61.5) G1 Post-tx: 56.3 (51.0 to 61.5) G1 2 month followup: 49.8 (44.3 to 55.3) G2 Pre-tx: 62.5 (57.6 to 67.4) G2 Post-tx: 51.7 (46.5 to 56.8) G2 2 month followup: 50.6 (45.4 to 55.8) Between group mean difference at post-tx: -2.35, p=0.37 Between group mean difference at 2 month followup: -7.89 p= 0.004 Treatment x time interaction at 2 months: F = 4.75, P =0.03 Clinically significant improvement: G1 Post-tx: 33 (63.5%) G2 Post-tx: 28 (49.1%) G1 2 month followup: 30 (66.7%) G2 2 month followup: 30 (54.5%) Between group mean difference at Post-tx: 14.3%, p = 0.13 Between group mean difference at 2 month followup: 42.1%, p=0.22	PCL Mean (95% CI) G1 Pre-tx: 63.6 (60.6 to 66.7) G1 Post-tx: 55.7 (52.6 to 58.9) G1 2 month followup: 55.4 (51.2 to 57.6) G1 Pre-tx: 58.8 (55.7 to 61.8) G2 Post-tx: 55.8 (52.7 to 58.9) G2 2 month followup: 56.0 (52.9 to 59.0) Between group mean difference at posttreatment: -4.95, p =0.002 Between group mean difference at 2 month followup: -6.44, t = 4.08, P <0.001 Group x time interaction at 2 months: F= 8.78, P=0.004 Clinically significant improvement: G1 Post-tx: 19 (36.5%) G2 Post-tx: 13 (22.8%) G1 2 month followup: 23 (48.9%) G2 2 month followup: 16 (28.1%) Between group mean difference at Post-tx: 13.7%, p =0.12 Between group mean difference at 2 month followup: 20.9%, p= 0.03	Loss of CAPS diagnosis, n (%) G1 Post-tx: 22 (42.3%) G1 2 month followup: 24 (53.3%) G2 Post-tx: 25 (43.9%) G2 2 month followup: 26 (47.3%) Post-tx, Between group mean difference: 1.6%, chi-sq = .03, p=0.87 2 month followup, Between group mean difference: 6%, chi-sq = .36, P=0.55 Remission NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Raskind et al., 2003[74]	G1: Prazosin 2 to 10 mg/day G2: Placebo	CAPS G1 Pre-tx:79.1 (17.0) G1 Post-tx: 57.3 (32.3) G2 Pre-tx: 83.6 (17.6) G2 Post-tx: 86.5 (30.0) G1 vs. G2 Change, p<0.01	NR	NR NR
Raskind et al., 2007[75]	G1: Prazosin 2 to 15 mg at bedtime G2: Placebo	CAPS Means (SD) G1 Pre-tx: 76.0 (22) G1 Post-tx: 63.0 (20.0) G2 Pre-tx: 78.0 (18.0) G2 Post-tx: 71.0 (22.0) G1 vs. G2 Change, NS	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Raskind et al., 2013[76]	G1: Prazosin 1 to 5 mg/day morning dose, 1 to 20mg/day bedtime dose G2: Placebo	CAPS Adjusted Means (95% CI) G1 Pre-tx: 77.3 (69.1 to 85.5) G1 Post-tx: 52.2 (43.8 to 60.5) Mean Change: 25.1 (SE = 3.4) G2 Pre-tx: 85.7 (78.0 to 93.3) G2 Post-tx: 71.9 (63.9 to 79.8) Mean Change: 13.8 (SE = 3.3) Between Group Difference in Change from Baseline: 11.3 (2.0 to 20.7), t = 2.39, p = 0.02 Subgroup Analysis Week-by-Treatment group-by-SSRI use Interaction for CAPS, p = 0.0007 Change in CAPS between baseline and week 15 (G1 only) Prazosin Not Receiving SSRI: 30.1 point decrease (SE =3.8) Receiving SSRI: 9.6 point decrease (SE=6.8)	NR	CGI Adjusted Means (95% CI) G1 Post-tx: 2.3 (1.8 to 2.7) G2 Post-tx: 3.2 (2.8 to 3.6) Between Group Difference in Change from Baseline: 0.9 (0.3 to 1.5), t = 3.13, p = 0.003 Treatment by SSRI use Interaction for CGI change NS Responders (CGI change item markedly or moderately improved=scores of 1 or 2) G1: 64% (44 to 79) G2: 27% (14 to 45) Difference in % responders, p<,0.001, OR = 4.8, (1.9 to 12.2) Full Remission (CAPS <20) G1: 3 G2: 0 Loss of PTSD diagnosis NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Reger et al., 2016[18]	G1: VRE G2: PE G3: WL (minimum attention)	CAPS (week) Mean (SD) G1 Pre-tx: 80.44 (16.23) G1 Post-tx: 57.07 (32.32) G1 12 week: 56.64 (31.50) G1 26 week: 53.50 (28.07) G2 Pre-tx: 78.28 (16.35) G2 Post-tx: 44.28 (33.73) G2 12 week: 36.63 (31.80) G2 26 week: 38.33 (28.49) G3 Pre-tx: 78.89 (16.87) G3 Post-tx: 68.06 (24.27) G1 vs. G3 Post-tx Differences: -13.23 (95% CI, -23.22 to -3.23), p <0.005, ES = -0.81 (95% CI, -1.42 to -0.20) G2 vs. G3 Post-tx Differences: -21.30 (95% CI, -31.60 to -12.19), p <0.001, ES = -1.33 (95% CI, -1.93 to -0.74) G1 vs. G2 Post-tx Differences: 8.67 (95% CI, -1.86 to 19.20), p = 0.947, ES = 0.53 (95% CI, -0.11 to 1.17) G1 vs. G2 12 week Differences: 14.50 (95% CI, 3.24 to 25.76), p = 0.994, ES = 0.88 (95% CI, 0.20 to 1.57) G1 vs. G2 26 week Differences: 13.68 (95% CI, 1.45 to 25.91), p = 0.986, ES = 0.83 (95% CI, 0.09 to 1.58)	PCL-C Mean (SD) G1 Pre-tx: 61.85 (9.03) G1 Post-tx: 45.57 (15.88) G1 12 week: 46.96 (15.95) G1 26 week: 42.88 (15.96) G2 Pre-tx: 59.74 (9.09) G2 Post-tx: 40.63 (18.57) G2 12 week: 38.41 (17.98) G2 26 week: 40.83 (18.56) G3 Pre-tx: 60.30 (8.97) G3 Post-tx: 53.89 (11.77) G1 vs. G3 Post-tx Differences: -11.33 (95% CI, -16.18 to -6.48), p <0.001, ES = -1.26 (95% CI, -1.79 to -0.72) G2 vs. G3 Post-tx Differences: -11.23 (95% CI, -15.93 to -6.54), p <0.001, ES = -1.25 (95% CI, -1.77 to -0.72) G1 vs. G2 Post-tx Differences: -0.10 (95% CI, -5.18 to 4.98), p = 0.485, ES = -0.01 (95% CI, -0.57 to 0.55) G1 vs. G2 12 week Differences: 2.86 (95% CI, -2.58 to 8.29), p = 0.849, ES = 0.32 (95% CI, -0.29 to 0.92) G1 vs. G2 26 week Differences: -0.06 (95% CI, -6.02 to 5.90), p = 0.492, ES = -0.01 (95% CI, -0.67 to 0.65)	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Reich et al., 2004[84]	G1: Risperidone 0.5 to 8 mg/day G2: Placebo	CAPS-2 Mean Changes from Baseline Score (SD) G1: -29.6 (31.5) G2: -18.6 (12.3) p=0.015	NR	NR NR
Resick et al., 2002[3] Resick et al., 2003[125] Resick et al., 2012[126]	G1: CBT, cognitive processing therapy G2: CBT, exposure-based therapy (PE) G3: WL	CAPS Mean (SD) G1 Pre-tx: 74.76 (18.77) G1 Post-tx: 39.08 (31.12) G1 3 mth FU: 42.21 (30.13 G1 9 mth FU: 42.87 (31.06) G1 LTFU: 26.00 (23.35) G2 Pre-tx:76.60 (19.72) G2 Post-tx: 44.89 (33.52) G2 3 mth FU: 49.16 (32.86) G2 9 mth FU: 46.98 (33.68) G2 LTFU: 25.90 (26.05)G3 Pre-tx: 69.85 (19.57) G3 Post-tx: 69.26 (18.55) G3 3 mth FU: 69.26 (18.55) G3 9 mth FU: 69.26 (18.55) Posttreatment differences, p<.0001 3 mth FU differences, p<0.0001 9 mth FU differences, p<0.0001 LTFU differences, NS	PSS Mean (SD) G1 Pre-tx: 29.55 (8.62) G1 Post-tx:13.66 (11.05) G1 3 mth FU: 14.67 (11.79) G1 9 mth FU:15.13 (12.03) G1 LTFU: 9.68 (10.38) G2 Pre-tx: 30.09 (9.18) G2 Post-tx:17.99 (13.17) G2 3 mth FU:18.05 (13.78) G2 9 mth FU: 18.40 (13.98) G2 LTFU: 9.89 (10.52) G3 Pre-tx: 28.70 (7.33) G3 Post-tx: 27.77 (8.12) G3 3 mth FU: 27.77 (8.12) G3 9 mth FU: 27.77 (8.12) Only G1 vs. G2 Posttreatment differences, NS 3 mth FU differences, NS 9 mth FU differences, NS LTFU differences, p=0.06	NR Lost of PTSD Dx at Posttreatment G1: 53% G2: 53% G3: 2.2% G1 vs. G2 Overtime, NS LTFU G1: 81.6 G2: 58.7 G1 vs. G2, NS

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Resick et al., 2015[127, 128]	G1: CPT-C (Includes only the cognitive component of CPT) G2: PCT	PSS-I Mean (adjusted for pre-tx values at post-tx, 6 month, and 12 month followup) (SE) G1 Pre-tx: 27.7 (7.4) G1 Post-tx: 23.0 (1.3) G1 6-month followup: 20.0 (1.5) G1 12-month followup: 19.0 (1.4) G2 Pre-tx: 27.1 (7.0) G2 Post-tx: 23.9 (1.3) G2 6-month followup: 21 (1.5) G2 12-month followup: 19.9 (1.4) Between group differences at Post-tx: t = 0.53, p = .60 Between group difference at 6-month followup: t = 0.46, p = 0.65 Between group differences at 12-month followup: t = 0.45, p = 0.66	PCLS-S Mean (SD for Pre-tx and SE for Post assessments) Mean (SE) G1 Pre-tx: 59.3 (10.1) G1 Post-tx: 47.8 (1.9) G1 6-month followup: 46.8 (2.0) G1 12-month followup: 46.1 (2.3) G2 Pre-tx: 58.5 (10.6) G2 Post-tx: 51.2 (1.9) G2 6-month followup: 50.2 (2.0) G2 12-month followup: 48.6 (2.2) Slope (SE) and p value for ME regression model of PCLS-S with repeated measures. G1: -1 (.11), t = -8.98, p < .0001 G2: -.6 (.11), t = -5.49, p < .0001 Difference: -.4 (.16), t = 2.55, p = .012 Between group effect sizes (d): Baseline to posttreatment: -.4 Baseline to 6 months: -.4 Baseline to 1 year: -.3	NR
Rothbaum et al., 1997[45]	G1: EMDR G2: WL	PSS Mean (SD) G1 Pre-tx: 33.3 (8.7) G1 Post-tx: 14.3 (8.4) G1 3 mth FU: 9.8 (8.7) G2 Pre-tx: 39.0 (8.2) G2 Post-tx: 35.0 (5.9) Posttreatment G1 vs. G2, p<0.05	IES Mean (SD) G1 Pre-tx: 47.4 (15.0) G1 Post-tx: 12.4 (11.2) G1 3 mth FU: 5.7 (5.8) G2 Pre-tx: 48.9 (8.9) G2 Post-tx: 45.4 (6.4) Posttreatment G1 vs. G2, p<0.01	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Rothbaum et al., 2005[13]	G1: CBT, exposure-based therapy (PE) G2: EMDR G3: WL	Data reported in graphs	Data only presented in graphs	NR Loss of PTSD Dx at Posttreatment: G1: 95% G2: 75% G3: 10% G1&G2 vs. G3 p<0.001 G1 vs. G2 p=0.108 Loss of PTSD Dx at 6 months f/u: G1: 94.4% G2: 73.7% p=0.185

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Ruglass et al., 2017 [143]	G1: COPE G2: Relaspe Prevention G3: AMCG	CAPS-Severity Mean (SD) G1 Pre-tx: 55.38 (16.40) G1 Post-tx: 37.63 (23.76) G1 Followup 1 months: 29.50 (27.88) G1 Followup 2 months: 29.77 (26.14) G1 Followup 3 months: 28.40 (23.09) Change at 1 month: -27.12 (95% CI, -35.84 to -18.40), p <0.001 Change at 3 months: -28.31 (95% CI, -36.01 to -20.60), p <0.001 G2 Pre-tx: 57.70 (20.80) G2 Post-tx: 30.79 (27.54) G2 Followup 1 months: 29.00 (22.99) G2 Followup 2 months: 30.40 (22.83) G2 Followup 3 months: 28.91 (22.91) Change at 1 month: -25.38 (95% CI, -33.12 to -17.64), p <0.001 Change at 3 months: -26.71 (95% CI, -34.28 to -19.14), p <0.001 G3 Pre-tx: 46.39 (11.07) G3 Post-tx: 41.89 (24.52) Change: NR, ns Treatment X Time interactions at 1-month, p = 0.86 In Group and Between Group Differences at 1 month and 3 months, ns	MPSS-SR Mean (SD) G1 Pre-tx: 54.26 (24.60) G1 Post-tx: 19.40 (17.70) Change: -42.99 (95% CI, -56.30 to -29.68), p <0.001 G2 Pre-tx: 57.49 (24.33) G2 Post-tx: 26.80 (20.87) Change: -31.51 (95% -40.64 to -22.38) G3 Pre-tx: 50.21 (23.58) G3 Post-tx: 40.00 (28.10) Change: NR, ns Treatment X Time Interaction, p <0.001 Between group differences G1 vs G3: -34.06 (95%CI -51.36 to -16.75), p <0.001 G2 vs G3: -22.58 (95%CI -36.92 to -8.24), p =0.002 G1 vs G2: -11.48 (95%CI -27.62 to 4.67), p =0.16	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Sannibale et al. 2013[146]	G1: IT (Integrated CBT for PTSD and AUD) G2: AS, (CBT for AUD plus supportive counseling)	CAPS-Severity Mean (SD) G1 Pre-tx: 68.00 (23.63) G1 Post-tx: 42.80 (26.45) G1 Followup 5 months: 40.39 (23.49) G1 Followup 9 months: 43.30 (28.25) G2 Pre-tx: 68.07 (21.10) G2 Post-tx: 46.71 (26.27) G2 Followup 5 months: 49.71 (22.90) G2 Followup 9 months: 41.19 (34.17) Treatment group*time interactions ns	PDS Mean (SD) G1 Pre-tx: 33.07 (10.43) G1 Post-tx: 21.88 (14.66) G1 Followup 5 months: 20.88 (13.37) G1 Followup 9 months: 22.88 (16.68) G2 Pre-tx: 31.38 (10.43) G2 Post-tx: 24.18 (14.05) G2 Followup 5 months: 24.48 (16.00) G2 Followup 9 months: 20.81 (17.00) Treatment group*time interactions ns	Remission NR Loss of Diagnosis based on CAPS, n (%) G1 Post-tx:20 (67) G1 Followup 5 months: 22 (73) G1 Followup 9 months: 21(70) G2 Post-tx: 21 (75) G2 Followup 5 months: 18(64) G2 Followup 9 months: 21 (75) Between group differences, β = -0.30, SE = 0.51, p = 0.554
Sautter et al., 2015[131]	G1: SAT G2: PFE	CAPS Mean (SE) G1 Pre-tx: 85.93 (3.31) G1 Post-tx: 48.33 (3.71) G1 12 week followup: 44.64 (3.78) G2 Pre-tx: 82.93 (3.37) G2 Post-tx: 72.59 (3.79) G1 12 week followup: 71.93 (3.86) Treatment X Time Interaction at post-tx, t (80) = 4.95, p <0.0001 Treatment X Time Interaction at 12 week followup, t (80) = 5.41, p <0.0001	PCL-M Mean (SE) G1 Pre-tx: 60.84 (2.12) G1 Post-tx: 42.16 (2.38) G1 12 week followup: 39.54 (2.48) G2 Pre-tx: 60.81 (2.17) G2 Post-tx: 53.91 (2.48) G2 12 week followup: 51.77 (2.53) Treatment X Time Interaction at post-tx, p = 0.0007 Treatment X Time Interaction at 12 week follow, p =0.0006	Remission/No Longer Met PTSD diagnostic criteria (based on CAPS lower than 45) at followup G1: 15 (52%) G2: 2 (7%) X2 (1) = 11.48, p = 0.0003 (Fisher's exact test)

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Schnurr et al., 2003[139]	G1: Exposure-based, trauma-focused group therapy (psychoeducation, cognitive restructuring, relapse prevention, and coping skills training) G2: Present-centered group Therapy (avoided trauma-focused references, cognitive restructuring, and other trauma-focused group therapy components)	CAPS Mean (SE) G1 Pre-tx: 80.41 (1.45) G1 7 mth FU: 74.00 (1.32) G1 12 mth FU: 72.79 (1.51) Change at 7 mths, p<0.001 Change at 12 mths, p<0.001 G2 Pre-tx: 82.01 (1.44) G2 7 mth FU: 76.03 (1.32) G2 12 mth: 74.82 (1.49) Change at 7 mths, p<0.001 Change at 12 mths, p<0.001 Treatment Effect, p=0.29 Cohort Effect, p=0.01 Treatment X Cohort Effect, p=0.04 PTSD Checklist Mean (SD) G1 Pre-tx: 61.84 (0.91) G1 7 mth FU: 59.70 (0.84) G1 12 mth FU: 58.78 (0.89) Change at 7 mths, p<0.01 Change at 12 mths, p<0.01 G2 Pre-tx: 62.60 (0.94) G2 7 mth FU: 61.03 (0.84) G2 12 mth FU: 60.00 (0.88) Change at 7 mths, p>0.05 Change at 12 mths, p<0.05 Treatment Effect, NS Treatment X Cohort Effect, p=0.05	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Schnurr et al., 2007[138]	G1: CBT, exposure-based therapy (PE) G2: PCT	CAPS Baseline Mean (95% CI) G1: 77.6 (74.8 to 80.4) G2: 77.9 (75.1 to 80.6) Least Means (95% CI) Immediate posttreatment G1: 52.9 (47.7 to 58.0) G2: 60.1 (55.3 to 64.8) G1 vs. G2, P=.01 3 mth FU G1: 49.7 (44.7 to 54.7) G2: 56.0 (50.5 to 61.5) G1 vs. G2, P=.047 6-month G1: 50.4 (45.0 to 55.8) G2: 54.5 (49.3 to 59.7) G1 vs. G2, p =.21 Treatment Effect, p=0.03 Treatment X Time, p=0.37	PCL Baseline Mean (95% CI) G1: 58.2 (56.0 to 60.3) G2: 57.1 (55.0 to 59.2) Least Square Means (95% CI) Immediate posttreatment G1: 41.6 (38.4 to 44.9) G2: 48.9 (45.8 to 52.0) G2 G1 vs. G2, p<0.001 3-month G1: 43.5 (40.2 to 46.7) G2: 48.8 (45.3 to 52.4) at posttreatment G1 vs. G2, p<0.008 6-month G1: 44.6 (41.2 to 48.1) G2: 48.5 (45.2 to 51.8) G1 vs. G2, p =0.049 Treatment X Time, p=0.18	Total remission, CAPs score <20 G1: 15.2% G2: 6.9% OR (95% CI): 2.43 (1.10-5.37) Loss of diagnosis based on CAPS G1: 41.0% G2: 27.9% OR (95% CI): 1.80 (1.10-2.96)

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Schnyder et al., 2011[49]	G1: Eclectic psychotherapy BEP G2: WL (Minimal attention)	CAPS Mean (SD) G1 Pre-tx: 78.6 (16.0) G1 Post-tx: 60.8 (32.8) G1 6 mth FU: 58.1 (30.5) G2 Pre-tx: 73.4 (19.2) G2 Post-tx: 66.4 (20.0) Group Effect, p<0.01	NR	Remission Rates (CAPS score <20) Posttreatment G1: 12.5% (n=2) G2: 0.0% (n= 0) 6-month Followup G1: 18.8% (n=3) G2: 0.0% (n= 0) Lost of PTSD Diagnosis (CAPS Total Score of <50) Posttreatment G1: 12.5% (n=2) G2: 0.0% (n=0)
Simon et al., 2008[174]	G1: Paroxetine 12.5 to 62.5 mg/day G2: Placebo (Placebo and 5 additional sessions of PE)	SPRINT Mean (SD) G1 Pre-tx: 16.11 (8.99) G1 Improvement Post-tx: 2.33 (5.24) G2 Pre-tx: 17.00 (7.65) G2 Improvement Post-tx: 4.57 (7.24) p=NS	NR	Remission based on having a SPRINT score less than 6 at end point G1: 33% G2: 14% NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Sloan et al., 2012[17]	G1: Sertraline 25 to 200mg/day G2: Venlafaxiene 37.5 to 375mg/day Sertraline 25 to 200mg/day	CAPS Standardized mean gain (95% CI) G1 Post-tx:3.18 (2.20, 4.16) G2 Post-tx: -0.14 (-0.39, 0.12) Condition X Time -17.96 (95% CI, -13.04, -22.89) individuals in the WET condition reported sign. Greater decreases in PTSD symptom severity across time than individuals in WL(p<.001) Hedge's g (effect size): Post-tx: 3.49 FU: 2.18		Remission NR Loss of Diagnosis G1 Post-tx: 95% G2 Post-tx: 12% X^2 = 37.66, p <0.001 G1 18 week followup: 100% G2 18 week followup: 33% X2 = 22.49, p <0.001
Sonne et al., 2016[186]	G1: WET G2: WL	NR	HTQ (ITT) Mean (SE) G1 Pre-tx: 3.24 (0.04) G1 Post-tx: 3.02 (0.06) Difference: 0.22 (0.06), p <0.01, Effect size: 0.54 G2 Pre-tx: 3.18 (0.05) G2 Post-tx: 3.05 (0.06) Difference: 0.13 (0.06), p =0.02, Effect size: 0.32 Group difference for difference between pre- and post-treatment ratings: 0.09 (0.08), p = 0.27, Effect size: 0.22 Group differences at follow up: Regression coefficient, B = 0.07 (95% CI, -0.09 to 0.22), Beta-coefficient = 0.06, SE = 0.08, p = 0.40	Remission NR Loss of PTSD diagnosis NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Spence et al., 2011[30]	G1: CBT-mixed (Imaginal exposure, Coping skills, Cognitive processing) G2: WL	NR	PCL-C Mean (SD) G1 Pre-tx: 60.78 (10.03) G1 Post-tx: 44.78 (17.29) G1 3 mth FU: 43.17 (17.89) G2 Pre-tx: 57.00 (9.69) G2 Post-tx: 51.79 (12.51) G2 3 mth FU: NR Treatment effect at 8 weeks, p<0.03	Significant difference between groups at posttreatment for remission on PCL (p<0.01) Loss of diagnosis based on PCL at 3 months G1: 61% G2: NR
Stein et al., 2002[80]	G1: Olanzapine 10 to 20 mg G2: Placebo	CAPS Mean Change from Baseline (95% CI) G1: -14.8 (SD=14.16) p<.05 G2: -2.67 (SD=10.55) p<0.05	NR	NR NR
Tarrier et al., 1999[129] Tarrier et al., 1999[130]	G1: CBT, exposure-based therapy G2: CBT, cognitive restructuring, Cognitive Therapy	CAPS Global Severity Mean (SD) G1 Pre-tx: 71.14 (18.98) G1 Post-tx: 48.24 (30.25) G1 6 mth FU: 52.11 (23.78) G2 Pre-tx: 77.76 (14.95) G2 Post-tx: 50.82 (23.99) G2 6 mth FU: 50.21 (24.37) G1 vs. G2 differences, NS 12-Month Followup G1 Pre-tx: 71.76 (19.59) G1 12 mth FU: 45.16 (28.26) G2 Pre-tx:76.93 (15.40) G2 12 mth FU: 52.48 (24.09) G1 vs. G2 differences, NS	IES-I Mean (SD) G1 Pre-tx: 23.86 (8.24) G1 Post-tx: 16.39 (10.04) G1 6 mth FU: 15.85 (9.26) G2 Pre-tx: 26.73 (7.80) G1 Post-tx:17.91 (10.29) G2 6 mth FU: 17.72 (10.40) G1 vs. G2 differences, NS 12 Month Followup G1 Pre-tx:24.68 (7.47) G1 12 mth FU: 15.67 (9.16) G2 Baseline: 26.55 (7.78) G2 12 mth FU: 18.68 (9.24) G1 vs. G2 differences, NS	NR Percent of Patients who were no longer PTSD cases Posttreatment Overall: 50% G1: 59% G2: 42% 6-Months Overall: 52% G1: 52% G2: 52% 12-Months Overall: 61%

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Tarrier et al., 1999[129] Tarrier et al., 1999[130] (continued)			IES-A Mean (SD) G1 Pre-tx: 22.69 (9.24) G1 Post-tx: 14.89 (9.09) G1 6 mth FU: 17.70 (10.74) G2 Pre-tx: 26.21 (7.55) G2 Post-tx: 19.61 (10.09) G2 6 mth FU: 18.31(9.66) G1 vs. G2 differences, NS IES-A 12 Month Followup G1 Pre-tx: 23.00 (9.36) G1 12 mth FU:18.00 (11.36) G2 Pre-tx:26.21 (7.93) G2 12 mth FU: 20.68 (10.97) G1 vs. G2 differences, NS Penn Inventory Mean (SD) G1 Pre-tx: 47.28 (10.96) G1 Post-tx: 34.43 (14.69) G1 6 mth FU: 41.78 (12.50) G2 Pre-tx: 46.52 (12.98) G2 Post-tx: 36.09 (15.46) G2 6 mth FU: 37.24 (15.76) G1 vs. G2 differences, NS 12 Followup G1 Pre-tx: 47.52 (10.79) G1 12 mth FU: 41.04 (14.08) G2 Pre-tx: 47.03 (13.45) G2 12 mth FU: 38.39 (15.12) G1 vs. G2 differences, NS	

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Taylor et al., 2003[133]	G1: CBT, exposure-based therapy G2: EMDR G3: Relaxation Training	CAPS Data only reported in graphs Completers G1 Pre-Post changes, p<0.005 G2 Pre-Post changes, p<.001 G3 Pre-Post changes, p<0.005 Intent to Treat No significant differences	PTSD Symptom Severity Scale (part of PTDS) Intent to Treat Sample 3 treatments did not differ (p>0.05)	NR NR
ter Heide et al., 2016[43]	G1: EMDR G2: Stabilisation	CAPS G1 vs. G2, d = -0.04, NS	HTQ, DSM-IV G1 vs. G2, d = 0.20, NS HTQ, total G1 vs. G2, d = 0.29, NS	Remission CAPS Severity change N (%) Improvement (> 10 points) G1:13/32 (40.6) G2: 13/31 (41.9) Loss of Diagnosis based on CAPS N (%) Posttreatment G1 Post-tx:6 (19) G2 Post -tx: 9 (29) X2 (df) = 0.08 (1), p = 0.78
Tucker et al., 2001[65]	G1: Paroxetine 20 to 50mg/day G2: Placebo	CAPS-2 Adjusted Mean Differences (95% CI), G1 vs. G2 -10.6 (-16.2 to -5.0) TOP-8 Adjusted Mean Differences (95% CI), G1 vs. G2 -3.8 (-5.6 to -1.9)	DTS Adjusted Mean Differences (95% CI) G1 vs. G2 -12.6 (-18.8 to -6.4) p<0.001	CAPS-2 total score <20 29.4% vs. 16.5% achieved remission; OR, 2.29; 95% CI, 1.24 to 4.23; p=0.008 NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Tucker et al., 2003[175] Tucker et al., 2004[176]	G1: Citalopram 20 to 50 mg/day G2: Sertraline 50 to 200 mg/day G3: Placebo	CAPS Mean (SD) G1 Pre-tx: 91.0 (10.58) G1 Post-tx: 60.28 (26.15) G2 Pre-tx: 83.91 (17.28) G2 Post-tx: 42.09 (29.09) G3 Pre-tx: 94.20 (11.9) G3 Post-tx: 55.5 (29.07) Between group differences, NS	IES G1 Pre-tx: 50.04 G1 Post-tx: 24.65 G2 Pre-tx: 46.26 G2 Post-tx: 17.16 G3 Pre-tx: 53.8 G3 Post-tx: 20.57 Between group diffrences, p value NR	NR NR
Tucker et al., 2007[78]	G1: Topiramate 25 to 400mg/day; given 2 times a day G2: Placebo	CAPS Mean Percentage Change (SD) G1: -59.5 (35.9) G2: -45.5 (34.3) p=0.227 TOP-8 Mean Percentage Change (SD) G1: -67.9 (30.0) G2: -41.6 (37.8) p= 0.023	DTS Mean Percentage Change (SD) G1: -54.1(35.8) G2: -32.3(34.8) p=0.065	CAPS score <20, N G1: 8 G2: 4 p=0.295 NR
Van Dam et al., 2013[262]	G1: SWT plus TAU G2: TAU (regular intensive treatment program for SUD based on CBT)	NR	PDS Mean (SD) G1 Pre-tx: 30.4 (9.7) G1 Post-tx: 17.6 (12.0) G1 Followup 3 months: 23.5 (14.8) G2 Pre-tx: 28.3 (10.7) G2 Post-tx: 24.3 (9.1) G2 Followup 3 months: 21.7 (9.4) Treatment X time Interaction, $F(3,34) = 1.92$, $p = 0.132$, $\eta^2 = 0.059$	Full and Partial Remission (Remitted based on SCID), n (%) G1 Post-tx:9.2(48.2) G2 Post-tx: 1.8 (12) Between group difference not reported Full PTSD Remission, (Remitted based on SCID), n (%) G1 Post-tx: 2 (22) G2 Post-tx: 1.2 (10) Between-group difference in PTSD diagnostic status (p = 0.06), less patients were diagnosed with PTSD in G1 vs. TAU NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
van den Berg et al., 2015[16]	G1: PE G2: EMDR G3: WL	CAPS Mean (SD or 95% CI) G1 Pre-tx:69.6 (14.9) G1 Post-tx: 37.8 (31.2 to 44.3) G1 6 month FU: 36.7 (30.1 to 43.4) G1 vs. G3 Post-tx, Effect size: 0.78 t = -3.84, p <0.001 G1 vs. G3 6 month, Effect size: 0.63 t = -3.10, p =0.002 G2 Pre-tx: 72.1 (17.6) G2 Post-tx: 40.3 (33.6 to 47.1) G2 6 month FU: 38.8 (31.9 to 45.6) G2 vs. G3 Post-tx, Effect size: 0.65 t = -3.26, p =0.001 G2 vs. G3 6 month, Effect size: 0.53 t = -2.66, p =0.009 G3 Pre-tx: 68.1 (15.9) G3 Post-tx: 56.5 (49.5 to 63.6) G3 6 month FU: 51.9 (44.9 to 58.9) G1 vs. G2 differences NS	PSS-SR Mean (SD or 95% CI) G1 Pre-tx: 28.5 (8.0) G1 Post-tx: 16.1 (13.1 to 19.1) G1 6 month FU: 16.4 (13.4 to 19.4) G1 vs. G3 Post-tx, Effect size: 0.88 t = -4.33, p <0.001 G1 vs. G3 6 month, Effect size: 0.70 t = -3.46, p =0.001 G2 Pre-tx: 30.3 (7.8) G2 Post-tx: 16.1 (12.9 to 19.2) G2 6 month FU: 16.2 (13.0 to 19.3) G2 vs. G3 Post-tx, Effect size: 0.85 t = -4.26, p <0.001 G2 vs. G3 6 month, Effect size: 0.70 t = -3.51, p =0.001 G3 Pre-tx: 27.7 (8.9) G3 Post-tx: 25.8 (22.5 to 28.9) G3 6 month FU: 24.1 (20.9 to 27.4) G1 vs. G2 differences NS	Full Remission based on CAPS (score <20) N (%) G1 Post-tx: 15 (28.3) G2 Post-tx:9 (16.4) G3 post-tx:3 (6.4) G1 vs. G3 Post-tx, OR = 3.41, p = 0.006 G2 vs. G3 Post-tx, OR = 3.92, p < 0.001 G1 6 month FU: 14(26.4) G2 6 month FU: 8 (14.5) G3 6 month FU: 3 (6.4) G1 vs. G3 6 month FU, OR = 3.01, p = 0.003 G2 vs. G3 6 month FU, OR= 2.76, p = 0.002 G1 vs. G2 differences NS Loss of Diagnosis based on CAPS N (%) G1 Post-tx:30 (56.6) G2 Post-tx:33 (60.0) G3 post-tx: 13 (27.7) G1 vs. G3 Post-tx, OR = 3.01, p = 0.003 G2 vs. G3 Post-tx, OR = 2.76, p = 0.002 G1 6 month FU:31 (58.5) G2 6 month FU: 31 (56.4) G3 6 month FU:15 (31.9) G1 vs. G3 6 month FU, OR = 3.01, p = 0.003 G2 vs. G3 6 month FU, OR= 2.76, p = 0.002 G1 vs. G2 differences NS

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
van der Kolk et al., 1994[63]	G1: Fluoxetine 20 to 60mg/day G2: Placebo	CAPS Difference in Improvement G1 vs. G2= 12.59 ANCOVA Results F = -12.59, t = -2.67, p=0.0106	NR	NR NR
van der Kolk et al., 2007[47]	G1: EMDR G2: Fluoxetine 10 to 60 mg/day G3: Placebo	CAPS Mean (SD) (Post-tx & FU - ITT) G1 Pre-tx (1 mth CAPS): 71.7 (11.9) G1 Pre-tx (1 wk CAPS): 69.4 (12.7) G1 Post-tx: 32.55 (22.5) G1 FU: 25.79 (21.61) G2 Pre-tx (1 mth CAPS): 75.9 (15.6) G2 Pre-tx (1 wk CAPS): 73.7 (13.4) G2 Post-tx: 42.67 (22.11) G2 FU: 42.12 (15.83) G3 Pre-tx (1 mth CAPS): 74.5 (12.5) G3 Pre-tx (1 wk CAPS): 70.3 (13.0) G3 Post-tx: 43.55 (22.6) G3 FU: NA Posttreatment Treatment effect, NS G1 vs. G3, NS G2 vs G3, NS G1 vs. G2, NS Followup G1 vs. G2, p=0.005	NR	% asymptomatic, defined as CAPS <20 G1: 28 G2: 13 G3: 10 G1 vs. G2, p=0.17 G1 vs. G3, p=0.09 G2 vs. G3, p=0.72 6-month post-treatment f/u (intent-to-follow) G1: 58% G2: 0% G3: NA p<0.001 Lost of PTSD Diagnosis, % G1: 76 G2: 73 G3: 59 G1 vs. G2, p=0.82 G1 vs. G3, 0.16 G2 vs. G3, 0.23 (G2/3) 6-month post-treatment f/u (intent-to-follow) G1: 88% G2: 73% G3: NA p= 0.20

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
van der Kolk et al., 2016[162]	G1: Neurofeedback G2: WL	CAPS Mean (95% CI) G1 Pre-tx: 79.45 (72.86 to 86.04) G1 Post-tx: 42.95 (34.1 to 51.8) G1 1 month FU: 39.1 (29.69 to 48.51) G1 Pre-tx to 1 month difference: -40.42 (-48.67 to -32.12) d = -2.33 G2 Pre-tx: 76.24 (69.13 to 83.36) G2 Post-tx: 66.49 (57.39 to 75.6) G2 1 month FU: 65.46 (55.83 to 75.1) G2 Pre-tx to -1 month difference: -10.78 (-19.1 to -2.48) d = -0.62 Difference between groups at 1 month: -29.6 (-41.33 to -17.87) d = -1.71 Treatment x time interaction: b = -10.45, t = -5.1, p <0.001	DTS Mean (95% CI) G1 Pre-tx: 67.28 (57.55 to 77.00) G1 Post-tx: 44.19 (35.76 to 52.63) G1 1 month FU: 36.5 (27.4 to 45.6) G1 Pre-tx to post-tx difference: -23.04 (-29.68 to -16.48) d = -0.92 G1 Post-tx to FU difference: -7.69 (-9.89 to -5.49) d = -0.31 G2 Pre-tx: 62.97 (52.47 to 73.48) G2 Post-tx: 58.21 (49.26 to 67.16) G2 1 month FU: 56.62 (47.09 to 66.15) G2 Pre-tx to post-tx difference: -4.76 (-11.6 to 2.07) d = -0.19 G2 Post-tx to FU difference: -1.59 (-3.87 to 0.69) d = -0.06 Difference between groups at post-tx: -18.32 (-27.82 to -8.82) d = -0.73 Difference between groups at post-tx to FU: -6.11 (-9.27 to -2.94) d = -0.24 treatment x time interaction: b = -1.52, t = -3.89, p <0.001	Loss of PTSD Diagnosis, n (%) G1 post-tx: 72% G2 post-tx: 32% G1 1 month FU: 58% G2 1 month FU: 10% Posttx between group difference chi-sq: 7.38, p=0.007 Baseline between group difference chi-sq: 9.47, p = 0.002

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
van Emmerik et al., 2008[40]	G1: CBT-Mixed Psychoeducation, prolonged exposure, imaginal exposure, exposure in vivo, cognitive exposure G2: SWT G3: WL	NR	IES Mean (SD) G1 Pre-tx: 46.40 (12.32) G1 Post: 32.00 (20.32) G1 FU: 33.68 (22.18) G2 Pre-tx: 47.87 (13.82) G2 Post-tx: 34.32 (22.58) G2 FU: 33.68 (24.63) G3 Pre-tx: 49.14 (14.66) G3 Post-tx: 45.66 (13.65) G3 FU: 46.63 (13.17) Group X Time Effect G1 vs G2, p=0.62 G1+G2 vs G3, p<0.01	NR NR
Wells et al., 2014[19]	G1: Metacognitive therapy G2: PE G3: WL	NR	PDS Mean (SD) G1 Pre-tx: 37.2 (8.93) G1 Post-tx: 10.4 (6.98) G1 3 month FU: 14.5 (16.2) Mean difference, post-tx: 26.8 (SE, 2.2), p <.005, (95% CI, 21.82 to 31.78) G2 Pre-tx: 32.80 (8.85) G2 Post-tx: 18.3 (13.31) G2 3 month: 16.5 (9.47) Mean difference, post-tx: 14.5 (SE, 4.61), p = 0.01, (95% CI, 0.08 to 24.92) G3 Pre-tx: 38.3 (8.74) G3 Post-tx: 39.2 (8.85) G3 3 month: NA Mean difference, post-tx: -0.9 (SE, 0.75), p > 0.05, (95% CI, -2.60 to 0.80)	Loss of Diagnosis based on SCID-I/P G1: 1 (10%) G2:3 (33%) G3:NR Remission NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Wells et al., 2014[19] (continued)			Treatment X Time Interaction: F=21.70, p < .0005 Hedge's g: G1 Pre-Post: 3.52 G2 Pre-Post: .91 G1 Pre-FU: 1.23 G2 Pre-FU: 1.08 ANCOVA group effect: F = 25.79, p < .0005 G1 vs G3 Pre-Post: 28.16 (3.95), p < .0005, (95% CI, 18.05 to 38.28) G2 vs G3 Pre-Post: 17.71 (4.09), p = .001, (95% CI, 7.25 to 28.16) G1 vs G2 Pre-Post: 10.46 (4.05), p = .05, (95% CI, 0.13 to 20.79) ANCOVA group effects at followup G1 vs. G2: F = 0.16, p = 0.69 IES Mean (SD) G1 Pre-tx: 53.3 (8.87) G1 Post-tx: 9.9 (9.69) G1 3 month FU: 17.1 (19.31) Mean Difference, post-tx: 43.4 (SE, 2.77), p<0.0005, (95% CI, 37.13 to 49.68) G2 Pre-tx: 51.2 (8.16) G2 Post-tx: 23.7 (16.28) G2 3 month followup: 22.1 (16.21.19) Mean Difference, post-tx: 27.5 (SE, 5.91), p = 0.001, (95% CI, 14.13 to 40.87)	

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Wells et al., 2014[19] (continued)			G3 Pre-tx: 52.3 (12.98) G3 Post-tx: 51.3 (13.43) G3 3 month followup: NA Mean Difference, post-tx:1.0. (SE, 3.12), p >.05, (95% CI, -6.06 to 8.06) Treatment X Time: F = 26.3, p < 0.005 Hedge's g: G1 Pre-Post: 4.52 G2 Pre-Post: 1.34 G1 Pre-FU: 2.39 G2 Pre-FU: 1.17 ANCOVA group effect: F = 28.81, p < 0.0005 G1 vs G3 Pre-Post: 41.43 (SE, 5.60), p < 0.0005, (95% CI, 27.59 to 56.26) G2 vs G3 Pre-Post: 27.02 (SE, 5.60), p <0.0005, (95% CI, 12.68 to 41.36) G1 vs G2 Pre-Post: 14.9 (SE, 5.62), p = 0.04, (95% CI, 0.52 to 29.28) ANCOVA group effects at followup G1 vs. G2: F = 0.62, p = 0.44	
Yeh et al., 2011[79]	G1: Topiramate 25 to 200mg/day G2: Placebo	CAPS Mean(SD) G1 Pre-tx: 78.76 (12.64) G1 Post-tx: 30.41 (30.90) G2 Pre-tx: 66.14 (22.63) G2 Post-tx: 35.78 (33.76) Between Group Change, p=0.49	NR	NR NR

Author, Year	Intervention Groups	Clinician Administered	Self-Administered	Symptom Remission Loss of PTSD Diagnosis
Zlotnick et al., 2009[56]	G1: Seeking Safety; G2: Usual care Psychoeducational group and individual case management and drug counseling	CAPS Mean difference (95% CI) -2.30 (-13.81, 9.21)	NR	NR Percentage that Loss PTSD Diagnoiss based on CAPS Post-tx G1: 52 G2: 45 3 mth FU G1: 61 G2: 57 6 mth FU G1: 57 G2: 62
Zohar et al., 2002[72]	G1: Sertraline 50 to 200 mg/day G2: Placebo	CAPS-2 Mean Change from Baseline (SD) G1: -18.7 (6.7) G2: -13.5 (6.6) Between Group Change, p=0.530	NR	NR NR

AMCG = active monitoring control group; ANOVA = analysis of variance; ANCOVA = analysis of covariance; CAPS = Clinician-administered PTSD Scale; CBT = Cognitive behavioral therapy; CI = confidence interval; CT = cognitive therapy; CPT = cognitive processing therapy; CPT-SA = Cognitive Processing Therapy for Sexual Abuse Survivors; DTS = Davidson Trauma Scale; EMDR = Eye movement desensitization and reprocessing; FU = Folow-up; HLS = health information control condition; IES = Impact of Event Scale; IRT = imagery rehearsal therapy; mg = milligram; MVA = motor vehicle accident; NA = not applicable; NF = Neurofeedback; NR= not reported; NS = not significant; OR = odds ratio; PCL-C =Posttraumatic Stress Disorder Checklist-Civilian; PCL-M = Posttraumatic Stress Disorder Checklist-Military; PCLS = Posttraumatic Stress Disorder Checklist Scale; PDS = Posttraumatic Diagnostic Scale; PE= prolonged exposure; PTSD = post-traumatic stress disorder; Pre-tx = pretreatment; Post-tx = Posttreatment; PSS= PTSD Symptom Scale; PSS-SR= PTSD Symptom Scale-Self-report; PTSD= Post-Traumatic Stress Disorder; RMANOVA, repeated measures analysis of variance; SCID =; SD = standard deviation; SE = standard error; SI-PTSD or SIP= Structured Interview for PTSD; SPRINT= Short PTSD Rating Interview; SSRIs = Selective serotonin re-uptake inhibitors or serotonin-specific reuptake inhibitor; STAIR = Skills Training in Affect and Interpersonal Regulations; SWT = strutured writing therapy; TOP-8 = Treatment Outcome PTSD Scale; VRET = virtual reality exposure therapy.

Table F-2. Comorbid conditions, quality of life, impairment, and ability to return to work

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Acarturk et al., 2016[44]	G1: EMDR-R-TEP G2: WL	BDI-II Mean (SE at pre-tx; SD at post-tx and followup) G1 Pre-tx:29.85 (9.27) G1 Post-tx: 10.45 (1.73) G1 1 month followup: 12.85 (1.98) G2 Pre-tx: 28.53 (7.99) G2 Post-tx: 26.35 (1.68) G2 1 month followup: 26.13 (1.87) G1 vs G2 pre to posttreatment p<0.001 G1 vs G2 pretreatment to followup p<0.001 Treatment X Time, F = 0.76, p = 0.368 from posttreatment to followup Mean estimated difference, post-tx: -15.90 (95% CI, -20.20 to -11.09), p <0.001 Mean estimated difference, 1 month followup: -13.28 (95% CI, -18.73 to -7.82), p <0.001 HSCL Mean (SE at pre-tx; SD at post-tx and followup) G1 Pre-tx:2.65 (0.50) G1 Post-tx: 1.54 (0.09) G1 1 month followup: 1.73 (0.10) G2 Pre-tx: 2.46 (0.44) G2 Post-tx: 2.34 (0.09) G2 1 month followup: 2.34 (0.09)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Acarturk et al., 2016[44] (continued)		G1 vs G2 pre to posttreatment p<0.001 G1 vs G2 pretreatment to followup p<0.001 Treatment X Time, F = 1.79, p = 0.186 from posttreatment to followup Mean estimated difference, post-tx: -0.89 (95% CI, -1.15 to -0.64), p <0.001 Mean estimated difference, 1 month followup: -0.78 (95% CI, -0.96 to -0.43), p <0.001			
Acosta et al., 2017[149]	G1: Web CBT plus TAU (Thinking Forward and usual VA primary care services) G2: TAU, usual VA primary care services	Percent of drinking days Treatment by time effect, NS during treatment period, Estimate: -0.93 (1.12) Treatment by time effect, NS contrasting between in and post-treatment, Estimate: 1.67 (1.84) Percent of heavy drinking days Treatment by time effect, during treatment period, Estimate: -1.80 (0.79), p<0.05 Treatment by time effect, NS contrasting between in and post-treatment, Estimate: 1.89 (1.33) Percent of drug use days Treatment by time effect, NS during treatment period, Estimate: -0.27 (0.25) Treatment by time effect, NS contrasting between in and post-treatment, Estimate: -0.06 (0.49)	QOL – Physical domain Treatment by time effect, NS during treatment period, Estimate: 0.75 (0.52) Treatment by time effect, NS contrasting between in and post-treatment, Estimate: -0.51 (0.91) QOL – psychological domain Treatment by time effect, NS during treatment period, Estimate: 0.77 (0.58) Treatment by time effect, NS contrasting between in and post-treatment, Estimate: -0.88 (0.94) QOL – social domain Treatment by time effect, NS during treatment period, Estimate: 1.27 (1.02)	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Acosta et al., 2017[149] (continued)			Treatment by time effect, NS contrasting between in and post-treatment, Estimate: -2.00 (1.72) QOL – environment domain Treatment by time effect, NS during treatment period, Estimate: 0.13 (0.61) Treatment by time effect, NS contrasting between in and post-treatment, Estimate: 0.15 (1.02)		
Akuchekian et al., 2004[77]	G1: Topiramate 25 to 500 mg/day (sensitive patients started at 12.5mg/day) G2: Placebo	NR	NR	NR	NR
Asukai et al., 2010[10]	G1: CBT, exposure-based therapy G2: UC	CES-D Adjusted Means (SE) G1 Pre-tx:39.58 (3.53) G1 Post-tx: 20.30 (3.97) G2 Pre-tx:39.50 (3.52) G2 Pre-tx: 34.81 (3.65) At post: G1 vs. G2= p<0.05(based on t-test)	GHQ-28 Adjusted Means (SE) G1 Pre-tx:21.58 (1.89) G1 Post-tx: 10.04 (2.15) G2 Pre-tx:20.50 (1.89) G2 Post-tx: 17.65 (1.97) At post: G1 vs. G2= p<0.05(based on t-test)	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Bartzokis et al., 2005[86]	G1: Risperidone 1 to 3 mg/day G2: Placebo	HAM-A Unadjusted Change from baseline (SD) G1: -7.4 (5.7) G2:-2.0 (7.0) G1 vs. G2, p<0.001 HAM-D Unadjusted Change from baseline (SD) G1: -3.7 (8.0) G2: -1.4 (8.7) G1 vs. G2, p>0.05	NR	NR	NR
Basoglu et al., 2007[11]	G1: CBT, exposure-based therapy G2: WL	BDI Mean (SD) G1 Pre-tx:23.4 (5.9) G1 4 weeks:13.1 (6.2) G1 8 weeks: 13.3 (9.2) G2 Pre-tx:21.9 (3.5) G2 4 weeks: 20.5 (7.4) G2 8 weeks:18.4 (11.0) G1 vs. G2 at Week 4, p<0.01 G1 vs. G2 at Week 8, p<0.007	NR	Work and Social Adjustment Mean (SD) G1 Pre-tx: 4.1 (0.8) G1 4 weeks: 2.2 (1.4) G1 8 weeks: 1.7 (1.9) G2 Pre-tx: 4.1 (0.9) G2 4 weeks:3.3 (1.4) G2 8 weeks:2.7 (1.6) G1 vs. G2 at Week 4, p<0.01 G1 vs. G2 at Week 8, p<0.007	NR
Batki et al., 2014[165]	G1: Topiramate 25 to 300mg G2: Placebo	Alcohol consumption % Drinking Days Between-group analysis Weeks 1 to 12 Avg. G1: 19.5 (34.2) G2: 39.7 (36.5) P p = 0.036, IRR = 0.38, 95% CI 0.15 to-0.94, % diff. = 51 Main Effects of treatment, p = 0.063, IRR = 0.430; 95% CI = 0.18 to-1.05	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Batki et al., 2014[165] (continued)		%Heavy Drinking Days Between-group analysis Weeks 1 to 12 Avg. G1: 11.1 (27.1) G2: 16.8 (26.3) P p = 0.342, IRR = 0.56, 95% CI 0.17 -to 1.87, % diff. = 34 Standard Drinks per week Between-group analysis Weeks 1 to 12 Avg. G1: 8.7 (19.0) G2: 19.3 (30.5) P p = 0.099, IRR = 0.43, 95% CI 0.16 to-1.17, % diff. = 55 Drinks per Drinking Day Between-group analysis Weeks 1 to 12 Avg. G1: 1.9 (3.3) G2: 4.8 (6.5) P p = 0.057, IRR = 0.45, 95% CI 0.20 to-1.02, % diff. = 60 OCDS (Alcohol cravings) Between-group analysis Weeks 1 to 12 Avg. G1: 5.53 (6.55) G2: 11.08 (8.12) P p = 0.025, IRR = -7.02, 95% CI= -13.1 to 0.91, % diff. = 50 Main Effects of treatment, F (1,48) = 2.81, p = 0.100			

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Becker et al., 2007[183]	G1: Bupropion 100 to 300 mg/day G2: Placebo	BDI Within-Group Mean Change (SD) (Baseline-Endpoint) G1: 3.22 (4.77) G2: 3.61 (10.44) Group effect, p<0.05	NR	NR	NR
Blanchard et al., 2003[36]	G1: CBT-mixed G2: Supportive psychotherapy G3: WL	BDI Mean (SD) G1 Pre-tx: 24.3 (10.8) G1 Post-tx: 11.6 (12.3) G1 FU: 12.6 (13.5) G2 Pre-tx: 17.8 (13.0) G2 Post-tx: 56.3 (12.2) G2 FU: 17.8 (13.0) G3 Pre-tx: 25.2 (11.9) G3 Post-tx: 24.0 (12.1) Group X Time, Post-Tx G1 vs. G2 & G3 (Post-tx) (Group X Time), p<0.001 G2 vs G3 (Post-tx) (Group X Time), NS No changes at 3 mths	NR	GAF Mean (SD) G1 Pre-tx: 53.9 (11.4) G1 Post-tx: 75.8 (12.2) G1 FU: 74.7 (12.8) G2 Pre-tx: 56.0 (9.7) G2 Post-tx: 64.3 (13.4) G2 FU: 66.3 (15.1) G3 Pre-tx: 56.0 (13.1) G3 Post-tx: 60.4 (9.6) Group X Time, Post-Tx G1 vs. G2, p=0.001 G1 vs G3, p=0.001 G2 vs & G3, NS No changes at 3 months	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Blanchard et al., 2003[36] (continued)		State-Anxiety Mean (SD) G1 Pre-tx: 55.3 (14.1) G1 Post-tx: 38.9 (14.0) G1 FU: 42.6 (15.4) G2 Pre-tx: 56.3 (12.2) G2 Post-tx: 50.7 (12.6) G2 FU: 49.1 (14.5) G3 Pre-tx: 58.5 (10.9) G3 Post-tx: 58.8 (12.3) Group X Time, Post-tx G1 vs. G2 & G3, p<0.001 G2 vs. G3, significantly greater change for G2 Changes at 3 mths, NS Trait-Anxiety Mean (SD) G1 Pre-tx: 55.7 (14.0) G1 Post-tx: 41.0 (16.5) G1 FU: 40.6 (15.3) G2 Pre-tx: 56.7 (10.4) G2 Post-tx: 52.4 (12.3) G2 FU: 52.3 (12.6) G3 Pre-tx: 58.9 (10.1) G3 Post-tx: 57.7 (9.9) Group X Time, Post-Tx G1 vs. G2 & G3, p<0.001 G2 vs. G3, NS Changes at 3 mths			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Blanchard et al., 2003[36] (continued)		Global Severity Index Mean (SD) G1 Pre-tx: 70.1 (9.3) G1 Post-tx: 57.3 (12.6) G1 FU: 58.4 (14.3) G2 Pre-tx: 73.2 (6.4) G2 Post-tx: 67.6 (9.0) G2 FU: 65.3 (13.1) Group X Time, Post-tx G1 vs. G2 & G3, p<0.001 G2 vs. G3, significantly greater change for G2			
Boden et al., 2012[58]	G1: Seeking Safety and TAU G2: TAU	ASI Drug Use Mean (SD) G1 Pre-tx: 0.09 (0.08) G1 Post-tx: 0.06 (0.06) G1 6 mth FU: 0.05 (0.06) G2 Pre-tx: 0.11 (0.08) G2 Post-tx: 0.10 (0.09) G2 6 mth FU: 0.09 (0.09) Between Group Differences at Post-tx, p<0.05 Between Group Differences at 6 month FU, p<0.05 G1 Within-Group Differences Pre-tx vs. Post-tx, p<0.05 G1 Within-Group Differences Pre-tx vs. 6mth FU, p<0.05	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Boden et al., 2012[58] (continued)		Alcohol Use Mean (SD) G1 Pre-tx: 0.29 (0.26) G1 Post-tx: 0.17 (0.19) G1 6 mth FU: 0.14 (0.17) G2 Pre-tx: 0.23 (0.24) G2 Post-tx: 0.15 (0.13) G2 6 mth FU: 0.14 (0.15) Between Group Differences, NS G1 Within-Group Differences Pre-tx vs. Post-tx, p<0.05 G1 Within-Group Differences Pre-tx vs. 6 month FU, p<0.05 G2 Within-Group Differences Pre-tx vs. Post-tx, p<0.05 G2 Within-Group Differences Post-tx vs. 6 month FU, p<0.05			

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Bohus et al., 2013[23]	G1: DBT-PTSD G2: TAU-WL	BDI-II (ITT) Mean (SD) G1 Pre-tx: 38.00 (9.75) G1 Post-tx: 26.81(11.45) G1 18 week followup: 28.56 (10.62) G1 24 week followup: 29.47 (12.61) G2 Pre-tx: 39.53(9.13) G2 Post-tx: 40.55 (10.59) G2 18 week followup: 40.18 (11.10) G2 24 week followup: 37.87 (12.62) Hedges' g between group: 0.70 Treatment X Time Interaction: -0.223 (0.089), p<0.0135 SCL-90-Revised (ITT) Mean (SD) G1 Pre-tx: 1.90 (0.66) G1 Post-tx: 1.39(0.63) G1 18 week followup: 1.38 (0.63) G1 24 week followup: 1.41 (0.63) G2 Pre-tx: 2.01(0.58) G2 Post-tx: 1.94 (0.64) G2 18 week followup: 1.81 (0.70) G2 24 week followup: 1.73 (0.69) Hedges' g between group: 0.36 Treatment X Time Interaction: -0.002 (0.006), p=0.672	NR	GAF (ITT) Mean (SD) G1 Pre-tx: 41.50 (4.50) G1 Post-tx: 49.44(8.40) G1 18 week followup: 51.33 (7.88) G1 24 week followup: 51.08 (9.89) G2 Pre-tx: 42.79(7.19) G2 Post-tx: 43.79 (7.51) G2 18 week followup: 42.92 (8.00) G2 24 week followup: 42.92 (8.00) Hedges' g between group: 1.02 Treatment X Time Interaction: 0.503 (0.094), p<0.001	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Brady et al., 2000[66]	G1: Sertraline 25 to 200 mg/day G2: Placebo	HAM-D Mean Change (SEM) G1: -8.6 (1.3) G2: -5.0 (1.2) G1 vs. G2, p=0.04	Q-LES-Q Mean Change (SEM) G1: 11.7 (2.1) G2: 3.3 (16.7) G1 vs. G2, p=0.004	CAPS social functioning subscale Mean Change (SEM) G1:-1.2 (0.11) G2: -0.7 (0.11) G1 vs. G2, p=0.001 CAPS occupational functioning subscale Mean change(Endpoint – Baseline) (SEM) G1:-0.7 (0.10) G2: -0.4 (0.10) G1 vs. G2, p=0.001	NR
Brady et al., 2005[67]	G1: Sertraline 150 mg/day G2: Placebo	HAM-D ANOVA No significant between-group differences (p>0.05)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Bryant et al., 2003[41]	G1: CBT, exposure based therapy(PE) G2: CBT-Mixed Prolonged Imaginal Exposure plus CR G3: Supportive Control	STAI-State Mean (SD) G1 Pre-tx: 56.80 (11.22) G1 Post-tx: 43.10 (13.52) G1 6 mth FU: 42.85 (14.90) G2 Pre-tx: 54.60 (8.20) G2 Post-tx: 41.45 (14.77) G2 6 mth FU: 43.45 (11.85) G3 Pre-tx: 56.28 (11.12) G3 Post-tx: 51.50 (12.00) G3 6 mth FU: 53.33 (9.70) Post-tx, p<0.01 (main effects) FU, p<0.05 (main effect) BDI Mean (SD) G1 Pre-tx: 21.65 (11.18) G1 Post-tx: 17.45 (12.82) G1 6 mth FU: 16.15 (12.19) G2 Pre-tx: 23.15 (10.05) G2 Post-tx: 13.85 (14.31) G2 6 mth FU: 14.95 (13.99) G3 Pre-tx: 26.56 (11.15) G3 Post-tx: 23.78 (12.10) G3 6 mth FU: 25.33 (12.05) Post-tx, p<0.01 (main effect) FU, p<0.05 (main effect)	NR	Good End State Functioning at Followup (Being below specific cut-off scores for both PTSD and depression) G1: 15.0% G2: 40.0% G3: 0.0% G1 vs. G3, p<0.01 G1 vs. G2, p<0.07	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Bryant et al., 2008[42]	G1: CBT, exposure based (Imaginal Exposure) G2: CBT, exposure-based therapy (In vivo exposure) G3: CBT, exposure-based therapy (Imaginal Exposure/In vivo Exposure) G4: CBT-mixed Imaginal Exposure/In vivo Exposure/ cognitive restructuring	STAI Mean (SD) G1 Pre-tx: 59.10 (15.08) G1 Post-tx: 50.71 (16.36) G1 6 mth FU: 56.19 (16.03) G2 Pre-tx: 58.25 (15.62) G2 Post-tx:50.36 (18.68) G2 6 mth FU: 51.14 (17.88) G3 Pre-tx: 59.32 (12.75) G3 Post-tx:48.87 (16.74) G3 6 mth FU: 54.84 (15.44) G4 Pre-tx: 56.93 (12.75) G4 Post-tx: 46.46 (17.21) G4 6 mth FU: 46.89 (24.54) Post-tx, NS (main effect) 6 month FU, NS (main effect) BDI Mean (SD) G1 Pre-tx: 24.03 (10.81) G1 Post-tx: 21.31 (13.23) G1 6 mth FU: 20.58 (12.83) G2 Pre-tx: 25.38 (12.82) G2 Post-tx:19.36 (11.28) G2 6 mth FU: 19.79 (12.43) G3 Pre-tx: 24.23 (11.38) G3 Post-tx: 22.16 (15.44) G3 6 mth FU: 24.81 (14.90)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Bryant et al., 2008[42] (continued)		G4 Pre-tx: 21.79 (10.25) G4 Post-tx:13.96 (12.05) G4 6 mth FU: 13.54 (11.85) Post-tx, NS (main effect) 6 month FU, p<0.05 (main effect)			
Butterfield et al., 2001[82]	G1: Olanzapine 5 to 20mg/day G2: Placebo	NR	NR	SDS Mean (SD) G1 Pre-tx: 19.8 (7.9) G2 Post-tx: 12.1 (7.8) Change: -7.7 G2 Pre-tx: 21.6 (7.2) G2 Post-tx: 13.6 (8.7) Change: -8.0 G1 vs. G2, no group X time differences found	NR
Carey et al., 2012[81]	G1: Olanzapine 5 to 10mg G2: Placebo	MADRS Mean (SD) G1 Pre-tx: 15.9 (4) G1 Post-tx 8 week: 10.3 (6.8) G2 Pre-tx: 15.3 (2.9) G2 Post-tx 8 week: 15.3 (9.8) Week 8 G1 vs. G2, p = 0.137, Effect size, r = 0.29	NR	SDS Mean (SD) G1 Pre-tx: 18.3 (7.1) G1 Post-tx 8 week: 10.6 (6.9) G2 Pre-tx: 24.1 (4.2) G2 Post-tx 8 week: 20.6 (7.4) Week 8 G1 vs. G2, p = 0.004, Effect size, r = 0.57	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Carlson et al., 1998[46]	G1: EMDR G2: CBT, coping skills therapy (Biofeedback and general relaxation) G3: WL	BDI Mean (SD) G1 Pre-tx: 20.1 (7.5) G1 Post-tx: 6.9 (5.9) G1 3 mth FU: 8.6 (9.4) G1 9 mth FU:6.6 (5.9) G2 Pre-tx: 23.6 (10.8) G2 Post-tx: 15.8 (12.5) G2 3 mth FU: 18.3 (11.7) G2 9 mth FU:22.5 (12.1) G3 Pre-tx: 24.0 (9.9) G3 Post-tx: 23.5 (12.8) Post & 3 mths Group X Time, p<0.004 G1 vs. G3, p<0.01 (post) G1 vs. G2, NS (3 months) 9 month FU p<0.00 (t-test) STAI-State G1 Pre-tx: 47.2 (9.4) G1 Post-tx: 34.9 (9.0) G1 3 mth FU:40.6 (4.9) G2 Pre-tx: 58.2 (12.2) G2 Post-tx: 46.3 (13.3) G2 3 mth FU:47.7 G3 Pre-tx: 58.2 (10.5) G3 Post-tx: 51.4 (17.8) Post-tx & 3 mths Group X Time, NS 9 mo FU: DataNR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Carlson et al., 1998[46]		STAI-Trait Mean (SD) G1 Pre-tx: 54.0 (9.9) G1 Post-tx: 38.6 (9.7) G1 3 mth FU: 41.9 (6.9) G2 Pre-tx: 58.0 (9.1) G2 Post-tx: 50.8 (10.7) G2 3 mth FU: 51.8 (7.4) G3 Pre-tx: 61.7 (10.6) G3 Post-tx: 55.8 (11.2) Group X Time, p<0.06 Post-tx G1 vs. G3, p<0.001 G1 vs G2, p<0.01 3 month FU G1 vs. G2, p<0.01			

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Chard et al., 2005[2]	G1: CBT, cognitive processing therapy CPT-SA G2: WL	BDI-II Mean (SD) G1 Pre-tx: 24.43 (10.81) G1 Post-tx: 3.26 (4.75) G2 Pre-tx: 24.52 (11.55) G2 Post-tx: 22.41 (12.57) p<0.001	NR	NR	NR
Church et al., 2013[155]	G1: EFT, Emotional Freedom Techniques (brief exposure therapy combining cognitive and somatic elements, on PTSD and psychological distress symptoms in veterans) G2: WL	SA-45 GSI Mean (SE) G1 Pre-tx: 74.79 (1.4) G1 Post-tx: 58.51 (1.9) G2 Pre-tx: 72.39 (1.6) G2 Post-tx: 69.98 (1.4) Treatment X Time Interaction, p <0.0001 SA-45 PST Mean (SE) G1 Pre-tx: 72.74 (1.5) G1 Post-tx: 57.61 (1.9) G2 Pre-tx: 72.72 (1.5) G2 Post-tx: 70.42 (1.3) Treatment X Time Interaction, p <0.0001	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Cloitre et al., 2002[37]	G1: CBT, exposure-based therapy(STAIR) G2: WL	BDI Mean (SD) G1 Pre-tx:25 (10.6) G1 Post-tx: 8 (7.8) G2 Pre-tx:23 (9.0) G2 Post-tx: 22 (11.4) p<0.01 (interaction) STAI-S Mean (SD) G1 Pre-tx:57 (9.6) G1 Post-tx: 36 (8.6) G2 Pre-tx: 53 (15.6) G2 Post-tx: 55 (14.9) p<0.01 (interaction)	NR	SAS-SR Mean (SD) G1 Per-tx:2.44(0.29) G1 Post-tx:2.06 (0.40) G2 Pre-tx:2.57 (0.42) G2 Post-tx: 2.47 (0.53) p=0.02 (interaction)	NR
Cloitre et al., 2010[148]	G1: CBT-Mixed (STAIR) + PE G2: CBT-Mixed (STAIR) + Support (Skills Training) G3: Support (Skills Training) + PE	STAI Mean (SD) G1 Pre-tx:50.4 (9.41) G1 Post-tx:39.2 (9.92) G1 3 mth FU:38.8 (9.90) G1 6 mth FU:37.4 (10.72) G2 Pre-tx: 48.2 (12.45) G2 Post-tx: 42.9 (12.34) G2 3 mth FU: 41.8 (13.53) G2 6 mth FU:42.4 (12.66) G3 Pre-tx: 50.2 (10.85) G3 Post-tx:41.1 (12.13) G3 3 mth FU:51.8 (11.16) G3 6 mth FU: 47.5 (12.66)			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Cloitre et al., 2010[148] (continued)		p<0.003 (interaction) 3 mth FU G1 vs. G3, p<0.001 6 mth FU G1 vs. G3, p<0.003 BDI Mean (SD) G1 Pre-tx: 18.8 (10.01) G1 Post-tx: 8.9 (7.64) G1 3 mth FU: 9.8 (9.96) G1 6 mth FU: 7.9 (10.77) G2 Pre-tx: 21.1 (8.80) G2 Post-tx: 11.9 (8.54) G2 3 mth FU: 12.0 (8.75) G2 6 mth FU: 13.4 (8.84) G3 Pre-tx: 22.1 (10.60) G3 Post-tx: 12.9 (9.41) G3 3 mth FU: 14.2 (10.09) G3 6 mth FU: 13.6 (9.12) No treatment or interaction effects obtained for BDI	NR	NR	NR
Coffey et al., 2016[140]	G1: Modified PE+ Motivational enhancement therapy (met-ptsd), G2: PE as described in G1 without MET, relaxation prior to PE therapy. G3: HLS, relaxation prior to PE therapy	BDI-II Mean (95% CI) G1 Pre-tx: 32.40 (29.21, 35.69) G1 Post-tx: 10.78 (7.07, 14.50) G1 3month followup: 14.34 (9.82, 18.87) G1 6month followup: 13.39 (8.49, 18.30) G2 Pre-tx: 29.49 (26.48, 32.49) G2 Post-tx: 7.08 (3.49, 10.66)*			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Coffey et al., 2016[140] (continued)		G2 3 month followup: 10.21 (5.90, 14.51)* G2 6 month: 6.60 (2.16, 11.19)* G3 Pre-tx: 29.80 (26.61, 32.90) G3 Post-tx: 13.33 (9.89, 16.77) G3 3 month: 16.84 (12.94, 20.73) G3 6 month: 13.59 (8.97, 18.22) *Denotes significant improvement over HLS at alpha = .05 Treatment x time effect, post-tx: $X^2 = 5.16$, p = 0.08 Treatment x time effect, followup: $X^2 = 1.03$, p = 0.91 Cohen's d as compared with G3: G1 Post-tx: 0.22 G2 Post-tx: 0.26 G1 3 month followup: 0.18 G2 3 month followup: 0.48 G1 6 month followup: 0.006 G1 6 month followup: 0.46			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Coffey et al., 2016[140] (continued)		Alcohol PDA Mean (95% CI) G1 Pre-tx: 48.70 (41.82 to 55.57) G1 3 month followup: 92.46 (85.66 to 99.25) G1 6 month followup: 85.73 (78.94 to 92.52) G2 Pre-tx: 46.13 (39.04 to 52.61) G2 3 month followup: 97.32 (90.76 to 103.87) G2 6 month followup: 94.49 (87.94 to 101.05) G3 Pre-tx: 52.23 (45.53 to 59.03) G3 3 month followup: 97.08 (90.28 to 103.88) G3 6 month followup: 93.58 (86.78 to 100.37) Treatment x time effect, 3-month followup: $X^2 = 1.51$, $p = 0.47$ Treatment x time effect, 6 month followup: $X^2 = 1.11$, $p = 0.58$ Cohen's d as compared with G3: G1 3 month followup: 0.21 G2 3 month followup: 0.01 G1 6 month followup: 0.36 G2 6 month followup: 0.04	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Coffey et al., 2016[140] (continued)		Drug PDA Mean (95% CI) G1 Pre-tx: 45.47 (38.50 to 52.43) G1 3month followup: 93.37 (86.49 to 100.26) G1 6month followup: 91.97 (85.08 to 98.85) G2 Pre-tx: 53.44 (46.87 to 60.01) G2 3 month followup: 97.52 (90.87 to 104.16) G2 6 month: 96.94 (90.87 to 104.16) G3 Pre-tx: 59.59 (52.71 to 66.48) G3 3 month: 97.94 (91.06 to 104.83) G3 6 month: 91.70 (84.82 to 98.59) Treatment x time effect, 3-month followup: $X^2 = 0.92$, $p = 0.63$ Treatment x time effect, 6 month followup: $X^2 = 2.20$, $p = 0.33$ Cohen's d as compared with G3: G1 3 month followup: 0.24 G2 3 month followup: 0.02 G1 6 month followup: 0.21 G1 6 month followup: 0.02			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171]	G1: Fluoxetine 10 to 60mg/day G2: Placebo	NR	NR	SDS Week 12 difference (Baseline - Endpoint)(95% CI) G1 vs. G2 Difference: 6.2 (1.4 to 11.0), p<0.05 CHEF criterion of response Week 12 difference (Baseline - Endpoint)(95% CI) G1 vs. G2 Difference: 0.37 (0.17 to 0.57), p<0.001	NR
Cook et al., 2010[156]	G1: CBT, exposure-based therapy G2: Psychoeducation	BDI Mean (SD) G1 Pre-tx: 26.85 (11.82) G1 at 1 mth: 24.16 (13.35) G1 at 3 mths: 24.80 (13.14) G1 at 6 mths: 25.02 (13.30) G2 Pre-tx: 23.51 (11.92) G2 at 1 month: 22.31 (12.76) G2 at 3 mths:23.76 (12.76) G2 at 6 mths: 23.37 (12.34) Interactions, NS	SF-36 Mental Mean (SD) G1 Pre-tx:29.69 (9.08) G1 at 1 mth:32.33 (10.63) G1 at 3 mths: 30.98 (9.33) G1 at 6 mths:32.15 (8.99) G2 Pre-tx:34.52 (12.06) G2 at 1 mth:32.84 (9.75) G2 at 3mths: 34.00 (10.35) G2 at 6 mths: 34.78 (10.87) Interactions, NS		NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Cook et al., 2010[156] (continued)			SF-36 Physical Component Mean (SD) G1 Pre-tx: 37.17 (9.21) G1 1 mth:39.48 (10.19) G1 at 3 mths: 37.72 (9.57) G1 at 6mths: 35.80 (9.64) G2 Pre-tx: 38.53 (9.64) G2 Post-tx:36.84 (10.34) G2 at 3 mths: 35.96 (11.97) G2 at 6 mths: 37.21 (11.23) Interactions, NS		
Cottraux, 2008[31]	G1: CBT-mixed (Exposure in imagination or in vivo and cognitive therapy) G2: Supportive Control	HAM-A Post-tx (ITT analysis) G1 Mean Change from Baseline (SD): -11 (9) G2 Mean Change from Baseline (SD): -5.7 (8) Group effect, p=0.028 Interaction, p=NS 52 Weeks G1 Mean Change from Baseline (sd): -10.04 (11.18), G2 Mean Change from Baseline (sd): -8.79 (10.15), Interaction, p=0.73	Marks' Quality of Life Scale ITT analysis = NR Post-tx (completer analysis) G1 Mean Change from Baseline (SD): -6.66 (8.13) G2 Mean Change from Baseline (SD): -9.60 (7.98) p=0.26	Fear Questionnaire, Global Phobic Disability Subscale: ITT analysis = NR Post-tx (completer analysis) POST-TREATMENT G1 Mean Change from Baseline (SD): -2.14 (2.75) G2 Mean Change from Baseline (SDI): -2.00 (2.69) p=0.86	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Cottraux, 2008[31] (continued)		104 Weeks G1 Mean Change from Baseline (sd): -12.56 (11.29), p=NR G2 Mean Change from Baseline (sd): -17.00 (7.19), p=NR Interaction, p=0.30 Depression, BDI short form ITT = NR Completer Analysis (Post-tx): G1 Mean Change from Baseline (sd): -5.44 (6.15) G2 Mean Change from Baseline (sd): -4.66 (6.95), Interaction, p=0.70 52 WEEKS G1 Mean Change from Baseline (sd): -4.33(5.65), G2 Mean Change from Baseline (sd): -4.07 (5.80), Interaction, p=0.89 104 WEEKS: G1 Mean Change from Baseline (sd): -5.87 (6.66), p=NR G2 Mean Change from Baseline: -6.22 (5.84), p=NR Interaction, p=0.89			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Cottraux, 2008[31] (continued)			52 Weeks G1 Mean Change from Baseline (SD): -9.42 (9.36), p=NR G2 Mean Change from Baseline (SD): -7.64 (9.12), p=NR Interaction, p=0.57 104 Weeks G1 Mean Change from Baseline (SD): -10.00 (7.65), p=NR G2 Mean Change from Baseline (SD): -12.66 (8.23), p=NR Interaction, p=0.42	52 Weeks G1 Mean Change from Baseline (SD): -2.54 (2.90), p=NR G2 Mean Change from Baseline (SDI): -1.00 (2.48), p=NR Interaction, p=0.11 104 Weeks G1 Mean Change from Baseline (SD): -3.52 (2.79), p=NR G2 Mean Change from Baseline (SDI): -2.33 (2.82), p=NR Interaction, p=0.44	

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Davidson et al., 2001[68]	G1: Sertraline 50 to 200 mg/day G2: Placebo	HAM-D Change from Baseline to Endpoint (SD) G1: -7.7 (1.0) G2: -6.3 (1.0) p=0.33 (t-test) HAM-A Change from Baseline to Endpoint (SD) G1: -7.8 (0.8) G2: -6.4 (0.9) p=0.26 (t-test)	NR	NR	NR
Davidson et al., 2003[184]	G1: Mirtazapine 15 to 45 mg/day G2: Placebo	HADS-D Mean (SD) G1 Pre-tx: 10.2 (6.1) G1 Post-tx: 8.0 (6.0) G2 Pre-tx: 13.5 (4.3) G2 Post-tx: 13.0 (3.7) Treatment effect, p=0.08 HADS-A G1 Pre-tx: 11.8 (5.0) G1 Post-tx: 9.0 (5.8) G2 Pre-tx: 15.0 (3.3) G2 Post-tx 13.8 (3.7) Treatment effect, p<0.05	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Davidson et al., 2006[69]	G1: Venlafaxine 75 to 300mg/day G2: Sertraline 50 to 200mg/day G3: Placebo	HAM-D Mean Within-group difference (95% CI) G1: -7.09(-8.13 to -6.05) G2: -6.42 (-7.48 to - 5.37) G3: -5.54 (-6.58 to -4.50) Between group p-values based on pairwise comparisons from the analysis of variance model using baseline adjusted values G1 vs. G3: 0.039 G2 vs. G3: 0.244 G1 vs. G2: 0.379	Q-LES-Q-SF Mean Within-group difference (95% CI) G1: 11.54 (9.73 to 13.35) G2: 11.17 (9.30 to 13.04) G3: 8.75 (6.94 to 10.56) Between group p-values based on pairwise comparisons from the analysis of covariance model using baseline adjusted values G1 vs. G3: 0.033 G2 vs. G3: 0.068 G1 vs. G2: 0.782	GAF Mean Within-group difference (95% CI) G1: 14.16(12.16 to 16.16) G2: 13.63 (11.57 to 15.70) G3: 11.41 (9.32 to 13.49) Between group p-values based on pairwise comparisons from the analysis of covariance model using baseline adjusted values G1 vs. G3: 0.062 G2 vs. G3: 0.136 G1 vs. G2: 0.720 SDS Mean Within-group difference (95% CI) G1: -8.54 (-9.78 to -7.29) G2:-8.17 (-9.43 to -6.90) G3: -6.52 (-7.76 to -5.29) Between group p-values based on pairwise comparisons from the analysis of covariance model using baseline adjusted values G1 vs. G3: 0.025 G2 vs. G3: 0.068 G1 vs. G2: 0.683	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Davidson et al., 2006[73]	G1: Venlafaxine 37.5 to 300 mg/day G2: Placebo	HAM-D Between Group Mean Difference -1.4, p=0.007	Q-LES-Q-SF Between Group Mean Difference 3.7, p=0.007	SDS Between Group Mean Difference -2.0, p=0.03 GAF Between Group Mean Difference 3.3, p=0.03	
Davidson et al., 2007[166]	G1: Tiagabine 4 to16mg/day G2: Placebo	NR	NR	SDS Change from baseline (SD) G1: -5.5 (7.0) G2: -5.9 (7.7) p=0.74	NR
Davis et al., 2008[164]	G1: Divalproex 1000 to 3000 mg/day G2: Placebo	MADRS Mean (SD) G1 Pre-tx: 27.3 (8.5) G1 Post-tx:22.2 (10.6) G2 Pre-tx: 28.5 (7.1) G2 Post-tx: 24.0 (10.3) Diff b/t groups, p=NS HAM-A Mean (SD) G1 Pre-tx:24.1 (10.1) G1 Post-tx:19.4 (9.1) G2 Pre-tx: 22.8 (8.5) G2 Post-tx::20.1 (10.7) Diff b/t groups, p=NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ehlers et al., 2003[5]	G1: CT G2: Self-help booklet based on principles of CBT G3: Repeated assessments	BDI Mean (SD) G1 Pre-tx: 18.8 (6.7) G1 3 mth FU: 7.3 (6.3) G1 9 mth FU: 6.5(7.0) G2 Pre-tx: 22.9 (9.2) G2 3 mth FU: 16.1 (6.6) G2 9 mth FU: 15.2 (6.9) G3 Pre-tx: 22.7 (8.9) G3 3 mth FU: 17.1 (9.6) G3 9 mth FU: 12.0 (10.0) 3 mth FU Overall: p<0.001 G1 vs. G2, p<0.001 G1 vs. G3, p<0.001 9 mth FU Overall: p<0.001 G1 vs. G2, p<0.001 G1 vs. G3, p=0.02 BAI Mean (SD) G1 Pre-tx: 21.6 (7.9) G1 3 mth FU: 6.0 (5.8) G1 9 mth FU: 5.8 (4.9) G2 Pre-tx: 22.2 (9.9) G2 3 mth FU: 14.2 (8.9) G2 9 mth FU: 14.0 (8.6) G3 Pre-tx: 24.4 (7.4) G3 3 mth FU: 15.7 (10.4) G3 9 mth FU: 12.6 (8.6)	NR	SDS Mean (SD) G1 Pre-tx: 5.9 (2.4) G1 3 mth FU: 2.3 (2.8) G1 9 mth FU: 1.8 (2.5) G2 Pre-tx: 6.3 (2.0) G2 3 mth FU: 4.3 (2.5) G2 9 mth FU: 3.7 (2.2) G3 Pre-tx: 6.1 (1.9) G3 3 mth FU: 4.2 (1.9) G3 9 mth FU: 3.2 (2.7) 3 mth FU Overall: p<0.001 G1 vs.G2, p=0.001 G1 vs. G3, p<0.001 9 mth FU Overall: p=0.003 G1 vs. G2, p=0.001 G1 vs. G3, p= 0.007	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ehlers et al., 2003[5] (continued)		3 mth FU Overall: p<0.001 G1 v.s G2: p<0.001 G1 vs. G3: p<0.001 9 mth FU Overall: p<0.001 G1 vs. G2, p<0.001 G1 vs. G3, p<0.001			
Ehlers et al., 2005[8]	G1: CBT-mixed Cognitive therapy including restructuring and exposure G2: WL	BDI Mean (SD) G1 Pre-tx: 23.7 (9.0) G1 Post-tx: 10.6 (8.6) G1 6 mth FU: 11.2 (9.6) G2 Pre-tx: 23.2 (8.0) G2 Post-tx: 19.3 (7.2) G1 vs. G2, p=0.003 G1 Changes, p<0.0005 G2 Changes, p=0.025 BAI Mean (SD) G1 Pre-tx: 24.1 (11.1) G1 Post-tx: 8.2 (10.8) G1 6 mth FU: 7.5 (9.7) G2 Pre-tx: 19.2 (7.2) G2 Post-tx: 21.2 (11.2) G1 vs. G2, p<0.0005 G1 Changes, p<0.0005 G2 Changes, NS	NR	SDS Mean (SD) G1 Pre-tx: 7.6 (1.9) G1 Post-tx: 3.0 (2.6) G1 6 mth FU: 3.0 (2.6) G2 Pre-tx: 6.7 (1.9) G2 Post-tx: 6.3 (1.8) G1 vs. G2, p<0.0005 G1 Changes, p<0.0005 G2 Changes, NS	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ehlers et al., 2014[9]	G1: Intensive CT (standard CT delivered over a much shorter period) G2: Standard CT G3: Supportive Therapy G4: WL	BDI (ITT) Mean (SD) G1 Pre-tx: 23.93 (9.86) G1 6 weeks: 14.34 (9.30) G1 Post-tx:12.10 (9.97) G1 Followup 1 (27 weeks): 12.03 (11.25) G1 Followup 2 (40 weeks):12.84(12.54) Within-group pre-post effect, d= 1.19 G2 Pre-tx: 21.90 (10.77) G2 6 weeks: 13.39 (10.70) G2 Post-tx: 11.07 (11.80) G2 Followup 1 (27 weeks): 10.54 (12.70) G2 Followup 2 (40 weeks): 9.44 (12.18) Within-group pre-post effect, d = 0.96 G3 Pre-tx: 26.18 (10.68) G3 6 weeks: 19.79 (12.42) G3 Post-tx: 17.00 (12.82) G3 Followup 1 (27 weeks): 16.29(12.10) G3 Followup 2 (40 weeks): 18.60 (14.05) Within-group pre-post effect, d = 0.78 G4 Pre-tx: 23.47 (8.96) G4 6 weeks: 21.26 (8.06) G4 Post-tx: 20.85 (10.02) Within-group pre-post effect, d = 0.28	Quality of Life Enjoyment an Satisfaction Questionnaire (ITT) Mean (SD) G1 Pre-tx: 36.93 (12.84) G1 6 weeks: 49.54 (17.23) G1 Post-tx:52.67 (20.21) G1 Followup 1 (27 weeks): 58.10 (22.78) G1 Followup 2 (40 weeks):54.57(20.74) Within-group pre-post effect, d= 0.93 G2 Pre-tx: 39.36 (21.87) G2 6 weeks: 57.49 (20.82) G2 Post-tx: 62.93 (21.70) G2 Followup 1 (27 weeks): 60.43 (23.31) G2 Followup 2 (40 weeks): 65.11 (22.46) Within-group pre-post effect, d = 1.08 G3 Pre-tx: 38.78 (18.40) G3 6 weeks: 44.86 (25.25) G3 Post-tx: 49.22 (24.97) G3 Followup 1 (27 weeks): 49.61(25.67)	SDS (ITT) Mean (SD) G1 Pre-tx: 20.48 (5.55) G1 6 weeks: 10.72 (7.51) G1 Post-tx:9.30 (8.20) G1 Followup 1 (27 weeks): 10.61 (8.80) G1 Followup 2 (40 weeks):9.72(9.22) Within-group pre-post effect, d= 1.60 G2 Pre-tx: 21.39 (5.11) G2 6 weeks: 14.02 (9.35) G2 Post-tx: 10.02(9.76) G2 Followup 1 (27 weeks): 8.68 (9.50) G2 Followup 2 (40 weeks): 9.37 (10.07) Within-group pre-post effect, d = 1.50 G3 Pre-tx: 19.65 (6.97) G3 6 weeks: 16.60 (7.90) G3 Post-tx: 14.28 (9.09) G3 Followup 1 (27 weeks): 13.67(9.86) G3 Followup 2 (40 weeks): 14.47 (11.35 Within-group pre-post effect, d = 0.66 G4 Pre-tx: 17.28 (7.74) G4 6 weeks: 17.22 (6.67) G4 Post-tx: 17.20 (6.38) Within-group pre-post effect, d = 0.01	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ehlers et al., 2014[9] (continued)		Comparison of Treatment with Waitlist Treatment by time Interactions, F=5.16, df=3, 122.20, p<0.002 Between group effect sizes Adjusted Difference (95% CI) G1 vs. G4: 9.04 (4.26 to 13.81), p<0.001, d = 0.97 G2 vs. G4:8.81 (4.06 to 13.55), p<0.001, d= 0.95 G1 vs. G3: 3.49(-1.30 to 8.28), NS, d=0.37 G2 vs G3: 3.26 (-1.50 to 8.05), NS, d = 0.35 Interaction between condition and Linear time effects: F=0.79, df=2, 213.98, p > 0.23 BAI (ITT) Mean (SD) G1 Pre-tx: 26.23 (13.12) G1 6 weeks: 13.55 (12.16) G1 Post-tx:11.57 (11.94) Followup 1 (27 weeks): 10.37 (11.59) G1 Followup 2 (40 weeks):11.85(13.35) Within-group pre-post effect, d= 1.17 G2 Pre-tx: 28.42 (14.17) G2 6 weeks: 13.88(14.01) G2 Post-tx: 9.24 (12.09) G2 Followup 1 (27 weeks): 9.63 (13.71)	G3 Followup 2 (40 weeks): 50.38 (25.53) Within-group pre-post effect, d = 0.48 G4 Pre-tx: 45.68 (20.98) G4 6 weeks: 41.74 (15.13) G4 Post-tx: 46.75 (19.00) Within-group pre-post effect, d = 0.05 Comparison of Treatment with Waitlist Treatment by time Interactions, F=6.96, df=3, 106.85, p<0.002 Between group effect sizes Adjusted Difference (95% CI) G1 vs. G4: -12.43 (-21.28 to -3.58), p<0.01, d = 0.73 G2 vs. G4:-20.67 (-29.39 to -11.95), p<0.001, d= 1.21 G1 vs. G3: -4.45(-13.17 to 4.28), NS, d=0.26 G2 vs G3: -12.69 (-21.33 to -4.04), p<0.01, d = 0.74	Comparison of Treatment with Waitlist Treatment by time Interactions, F=14.01, df=3, 109.86, p<0.002 Between group effect sizes Adjusted Difference (95% CI) G1 vs. G4: 9.96(6.10 to 13.81), p<0.001, d = 1.33 G2 vs. G4: 9.82 (5.95 to 13.68), p<0.001, d= 1.30 G1 vs. G3: 5.51(1.71 to 9.31), p<0.01, d=0.74 G2 vs G3: 5.37 (1.59 to 9.15), p<0.01, d = 0.72 Interaction between condition and Linear time effects: F=7.45, df=2, 220.14, p = 0.001	

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ehlers et al., 2014[9] (continued)		G2 Followup 2 (40 weeks): 9.00 (12.61) Within-group pre-post effect, d = 1.46 G3 Pre-tx: 25.12 (11.31) G3 6 weeks: 17.01 (13.30) G3 Post-tx: 16.35 (14.56) G3 Followup 1 (27 weeks): 15.50(13.74) G3 Followup 2 (40 weeks): 15.99 (16.15) Within-group pre-post effect, d = 0.67 G4 Pre-tx: 23.57 (9.12) G4 6 weeks: 23.26 (10.88) G4 Post-tx: 22.13 (10.59) Within-group pre-post effect, d = 0.15 Comparison of Treatment with Waitlist Treatment by time Interactions, F=13.57, df=3, 106.85, p<0.002 Between group effect sizes Adjusted Difference (95% CI) G1 vs. G4: 11.98 (6.54 to 17.43), p<0.001, d = 1.13 G2 vs. G4:15.58 (10.04 to 20.91), p<0.001, d= 1.45 G1 vs. G3: 5.37(0.06 to 10.80), p <0.05, d=0.51 G2 vs G3: 8.86 (3.46 to 14.27), p<0.01, d = 0.83	Interaction between condition and Linear time effects: F=3.27, df=2, 231.98, p = 0.04		

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ehlers et al., 2014[9] (continued)		Interaction between condition and Linear time effects: F=5.40, df=2, 176.80, p = 0.005			
Engel et al., 2015[26]	G1: DESTRESS-PC (Delivery of Self Training and Education for Stressful Situations-Primary Care), a nurse guided online CBT and SIT G2: Optimized UC, usual primary care PTSD treatment augmented with low intensity care management, feedback to the primary care provider, and training of the clinic providers in management of PTSD.	PHQ-8 (Major Depression) Mean (SD) G1 Pre-tx: 13.53 (5.43) G1 Post-tx (6 weeks): 11.00 (6.65) G1 Post-tx (12 weeks): 9.66 (7.04) G1 Post-tx (18 weeks): 10.23 (7.01) G2 Pre-tx: 11.67 (4.65) G2 Post-tx (6 weeks): 10.24 (5.12) G2 Post-tx (12 weeks): 10.40 (6.77) G2 Post-tx (18 weeks): 8.96 (5.62) Treatment by time interaction, F(3, 186)=2.17, p=0.093 PHQ-15 (Somatic symptoms)Mean (SD) G1 Pre-tx: 13.25 (5.64) G1 Post-tx (6 weeks): 11.90 (5.63) G1 Post-tx (12 weeks): 11.37 (6.70) G1 Post-tx (18 weeks): 11.38 (6.16)	SF-36 Means NR Interaction terms, NS	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Engel et al., 2015[26] (continued)		G2 Pre-tx: 13.31 (5.04) G2 Post-tx (6 weeks): 11.86 (5.18) G2 Post-tx (12 weeks): 12.16 (6.80) G2 Post-tx (18 weeks): 10.79 (6.48) Interaction terms, NS			
Fecteau et al., 1999[38]	G1: CBT-mixed (Coping skills, exposure-therapy, and cognitive restructuring) G2: WL	BAI Mean (SD) G1 Pre-tx: 30.6 (7.4) G1 Post-tx: 15.8 (13.8) G2 Pre-tx: 34.8 (15.8) G2 Post-tx: 32.0 (13.3) Group effect, p-value <0.05 Follow up for G1 Only BAI G1 Pre-tx: 30.6 (7.4) G1 Post-tx: 15.8 (13.8) G1 3 mth FU: 16.9 (13.8) G1 6 mth FU: 16.8 (11.8) Change at 3 mths, p<0.05 (n = 10) Change at 6 mths, p<0.01 (n = 8) BDI Mean (SD) G1 Pre-tx: 26.3 (9.8) G1 Post-tx: 20.1 (17.1) G2 Pre-tx: 27.9 (10.5) G2 Post-tx: 24.7 (8.1)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Fecteau et al., 1999[38] (continued)		Group effect, NS Follow up for G1 Only BDI G1 Pre-tx: 26.3 (9.8) G1 Post-tx: 20.1 (17.1) G1 3 mth FU: 19.6 (15.6) G1 6 mth FU: 15.9 (11.0)** Change at 3 mths, NS (n = 10) Change at 6 mths, NS (n = 8)			
Foa et al., 1999[14] Zoellner et al., 1999[134]	G1: CBT, exposure-based therapy (PE) G2: CBT, coping skills therapy SIT G3: CBT-mixed Combined treatment (PE and SIT) G4: WL	BDI Mean (SD) G1 Pre-tx: 17.58 (11.29) G1 Post-tx: 5.75 (4.77) G1 3 mth FU: 8.02 (6.77) G1 6 mth FU: 6.85 (5.61) G1 12 mth FU: 6.15 (7.73) G2 Pre-tx: 21.73 (11.02) G2 Post-tx: 10.05 (8.06) G2 3 mth FU: 14.58 (12.16) G2 6 mth FU: 13.54 (12.51) G2 12 mth FU: 11.92 (14.48) G3 Pre-tx: 21.36 (10.51) G3 Post-tx: 10.49 (9.90) G3 3 mth FU: 13.65 (10.53) G3 6 mth FU: 10.00 (9.46) G3 12 mth FU: 11.88 (9.92) G4 Pre-tx: 25.21 (11.20) G4 Post-tx: 22.10 (14.97) Main Effect, p<0.01 G1 vs. G4, p<0.001 G2 vs. G4, p<0.05 G3 vs. G4, p<0.05	NR	Social Adjustment Scale - Global Mean (SD) G1 Pre-tx: 3.73 (0.83) G1 Post-tx: 2.45 (0.60) G1 3 mth FU: 2.58 (0.69) G1 6 mth FU: 2.33 (0.84) G1 12 mth FU: 2.69 (0.87) G2 Pre-tx: 3.79 (1.23) G2 Post-tx: 2.68 (1.00) G2 3 mth FU: 3.00 (1.37) G2 6 mth FU: 2.83 (1.10) G2 12 mth FU: 3.00 (1.30) G3 Pre-tx: 4.00 (1.11) G3 Post-tx: 2.95 (1.33) G3 3 mth FU: 3.37 (1.46) G3 6 mth FU: 2.94 (1.55) G3 12 mth FU: 3.13 (2.03) G4 Pre-tx: 3.93 (1.16) G4 Post-tx: 3.73 (1.10) Treatment Effect, p<0.05 G1 vs. G4, p<0.01 G2 vs. G4, p=0.08 G3 vs. G4, p=0.09 Active treatments did not differ from one another, p=0.14	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Foa et al., 1999[14] Zoellner et al., 1999[134] (continued)		G1 vs. G3, p<0.025 G1 vs. G2, p=0.06 STAI-State Mean (SD) G1 Pre-tx: 49.95 (13.70) G1 Post-tx: 32.43 (10.93) G1 3 mth FU: 37.16 (11.80) G1 6 mth FU: 34.95 (11.45) G1 12 mth FU: 34.84 (12.43) G2 Pre-tx: 51.50 (13.37) G2 Post-tx: 39.07 (11.55) G2 3 mth FU: 41.26 (14.02) G2 6 mth FU: 43.33 (17.01) G2 12 mth FU: 42.46 (16.98) G3 Pre-tx: 50.66 (15.37) G3 Post-tx: 40.55 (15.41) G3 3 mth FU: 43.74 (15.27) G3 6 mth FU: 41.12 (14.77) G3 12 mth FU: 38.75 (13.29) G4 Pre-tx: 51.44 (12.60) G4 Post-tx: 50.40 (13.80) Main Effect, p<0.01 G1 vs. G4, p<0.001 G2 vs. G4, p=0.11 G3 vs. G4, p=0.14 G2 vs. G3, NS G1 vs. G2, p<0.025 G1 vs. G3, p<0.01			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Foa et al., 2005[12]	G1: CBT, exposure-based therapy(PE) G2: CBT-mixed (PE plus CR) G3: WL	BDI Mean (SD) G1 Pre-tx: 26.1 (9.9) G1 Post-tx: 14.6 (13.8) G2 Pre-tx: 23.4 (9.3) G2 Post-tx: 13.8 (12.9) G3 Pre-tx: 23.6 (10.3) G3 Post-tx: 21.0 (10.7) Group X Time interaction, p<0.001 G1 vs. G3, p<0.05 G2 vs. G3, p<0.05 G1 vs. G2, ns	NR	Social Adjustment Scale - Work Mean (SD) G1 Pre-tx: 3.4 (1.2) G1 Post-tx: 2.8 (1.4) G2 Pre-tx: 3.2 (1.2) G2 Post-tx: 2.7 (1.4) G3 Pre-tx: 3.4 (1.5) G3 Post-tx: 3.5 (1.3) Group X Time interaction, p=0.059 Social Adjustment Scale-Social Mean (SD) G1 Pre-tx: 4.1 (1.0) G1 Post-tx: 3.5 (1.3) G2 Pre-tx: 4.0 (1.0) G2 Post-tx: 3.3 (1.2) G3 Pre-tx: 4.0 (1.2) G3 Post-tx: 3.8 (1.1) Group X Time interaction, ns	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Fonzo et al., 2017[137] Fonzo et al., 2017[21]	G1: PE G2: WL	BDI-II Mean (SD) G1 Pre-tx: 23.69 (8.68) G1 Post-tx: 9.69 (7.77) G2 Pre-tx: 23.17 (8.60) G2 Post-tx: 17.87 (9.27) Group X Time interaction, p=0.016	WHO QOL of BREF Mean (SD) Physical Health G1 Pre-tx: 12.46 (2.99) G1 Post-tx: 14.63 (3.29) G2 Pre-tx: 12.43 (3.11) G2 Post-tx: 12.65 (3.19) Group X Time interaction, p=0.039 Psychological Health G1 Pre-tx: 10.04 (2.29) G1 Post-tx: 13.19 (2.59) G2 Pre-tx: 10.83 (2.34) G2 Post-tx: 11.94 (2.52) Group X Time interaction, p=0.033 Social Relationships G1 Pre-tx: 9.71 (4.06) G1 Post-tx: 11.83 (3.20) G2 Pre-tx: 9.29(3.51) G2 Post-tx: 10.73 (3.20) Group X Time interaction, p=0.35 Environmental G1 Pre-tx: 12.30 (3.48) G1 Post-tx: 14.59 (2.42) G2 Pre-tx: 12.79 (3.37) G2 Post-tx: 13.57 (2.99) Group X Time interaction, p=0.22	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Forbes et al., 2012[4]	G1: CBT, CPT G2: TAU	BDI-II Mean (SD) G1 Pre-tx: 26.33 (11.38) G1 Post-tx:15.91 (11.97) G1 FU: 14.77 (12.86) G2 Pre-tx: 24.78 (11.99) G2 Post-tx: 20.83 (11.83) G2 FU: 19.11 (10.15) Change over time Post-tx, p=0.054 FU, p=0.785 STAI-Trait Mean (SD) G1 Pre-tx: 59.97 (13.52) G1 Post-tx: 44.59 (13.12) G1 FU: 43.59 (11.49) G2 Pre-tx: 50.29 (9.94) G2 Post-tx: 48.31 (12.75) G2 FU: 47.26 (16.17) Change over time Post-tx, p=0.018 FU, p=0.917	Abbreviated Dyadic Adjustment Scale (ADAS) Mean (SD) G1 Pre-tx: 25.84 (6.95) G1 Post-tx:27.41 (7.72) G1 FU: 25.81 (6.80) G2 Pre-tx: 28.73 (5.13) G2 Post-tx:26.15 (6.34) G2 FU: 27.98 (6.98) Change over time Post-tx, p=0.014 FU, p=0.025 World Health Organization Quality of Life Scale (WHO-QOL) WHOQOL-Physical Mean (SD) G1 Pre-tx: 19.68 (5.23) G1 Post-tx:21.23 (5.00) G1 FU:19.81 (5.38) G2 Pre-tx: 20.73 (4.69) G2 Post-tx:22.20 (4.90) G2 FU:20.39 (4.70)	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Forbes et al., 2012[4] (continued)			Change over time Post-tx, p=0.911 FU, p=0.453 WHOQOL-Psychological Mean (SD) G1 Pre-tx: 15.70 (4.34) G1 Post-tx:18.22 (4.59) G1 FU: 18.40 (4.66) G2 Pre-tx: 15.54 (3.56) G2 Post-tx: 16.23 (4.27) G2 FU: 16.35 (4.88) Change over time Post-tx, p=0.093 FU, p=0.955 WHOQOL-Social Mean (SD) G1 Pre-tx: 7.77 (2.78) G1 Post-tx: 8.43 (3.36) G1 FU: 8.97 (3.12) G2 Pre-tx: 8.46 (2.83) G2 Post-tx: 8.29 (2.20) G2 FU: 8.00 (2.38)		

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Forbes et al., 2012[4] (continued)			Change over time Post-tx, p=0.152 FU, p=0.197 WHOQOL-Environmental Mean (SD) G1 Pre-tx: 27.50 (4.53) G1 Post-tx: 28.73 (3.97) G1 FU: 28.16 (4.29) G2 Pre-tx: 29.07 (4.80) G2 Post-tx:28.40 (4.89) G2 FU: 28.14 (5.51) Change over time Post-tx, p=0.016 FU, p=0.738		

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ford et al., 2011[59]	G1: Trauma Affect Regulation: Guide for Education and Therapy (TARGET) G2: PCT G3: WL	BDI Mean (SD) G1 Pre-tx:16.0 (10.8) G1 Post-tx:11.6 (10.9) G2 Pre-tx:17.8 (10.2) G2 Post-tx:11.9 (10.1) G3 Pre-tx:17.8 (10.2) G3 Post-tx:11.9 (10.1) Group X Time Effect, p<0.01 STAI Mean (SD) G1 Pre-tx: 38.1 (13.0) G1 Post-tx: 31.4 (11.3) G2 Pre-tx:41.6 (13.0) G2 Post-tx:37.4 (13.3) G3 Pre-tx:43.0 (10.9) G3 Post-tx:42.6 (12.9) Group X Time Effect, p=0.19	NR	NR	NR
Ford et al., 2011[60]	G1: Trauma Affect Regulation: Guide for Education and Therapy (TARGET), G2: SGT	TSI Dissociation Symptoms Mean (SD) G1 Pre-tx: 14.5 (6.5) G1 Post-tx: 14.1 (6.4) G2 Pre-tx: 12.0 (6.0) G2 Post-tx: 9.1 (5.5) Treatment X Time Interaction at post-tx, F= 1.6, NS, d = -0.26 TSI Sexual Concerns Mean (SD) G1 Pre-tx: 9.6 (6.0) G1 Post-tx: 8.2 (7.3)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ford et al., 2011[60] (continued)		G2 Pre-tx: 6.1 (5.2) G2 Post-tx: 5.5 (4.7) Treatment X Time Interaction at post-tx, F= 0.5, NS, d = 0.22 TSI Sexual Behavior Problems Mean (SD) G1 Pre-tx: 9.2 (7.0) G1 Post-tx: 7.0 (7.4) G2 Pre-tx: 7.8 (7.4) G2 Post-tx: 6.6 (7.1) Treatment X Time Interaction at post-tx, F= 1.1, NS, d = 0.31 TSI Impaired Self-Reference Mean (SD) G1 Pre-tx: 14.8 (5.6) G1 Post-tx: 11.4 (5.6) G2 Pre-tx: 12.7 (6.2) G2 Post-tx: 11.4 (5.3) Treatment X Time Interaction at post-tx, F= 2.3, NS, d = 0.39 TSI Tension Reduction Behaviors Mean (SD) G1 Pre-tx: 9.3 (5.7) G1 Post-tx: 7.3 (5.1) G2 Pre-tx: 7.5 (5.3) G2 Post-tx: 6.6 (5.3) Treatment X Time Interaction at post-tx, F= 2.0, NS, d = 0.42			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Friedman et al., 2007[70]	G1: Sertraline 25 to 200 mg/day G2: Placebo	HAM-A Change at Endpoint (SE) G1: -4.1 (1.0) G2: -6.1 (1.1) Between Group Differences, NS HAM-D Change at Endpoint (SE) G1: -2.7 (1.1) G2: -4.2 (1.1) Between Group Differences, NS	NR	NR	NR
Galovski et al., 2012[6]	G1: Modified CBT. Modifications include potential addition of stressor sessions and variable length of treatment. G2: Delayed treatment symptom monitoring	BDI-II LSM (SE) G1 Pre-tx: 30.06 (1.53) G1 Post-tx: 9.67 (2.06) Difference: -20.2 G2 Pre: 32.50 (1.65) G2 Post: 25.51 (2.13) Difference: -7.0 (Hedge's g = .92) G1 vs. G2: -13.2, p < .001	QOLI LSM (SE) G1 Pre-tx LSM=1.18 (4.65) G1 Post-tx: 21.87 (5.69) Point Improvement: 20.7, p G2 Pre-tx: -.17 (4.81) G2 Post-tx: 3.05 (5.89) Point Improvement: 3.2 (Hedge's g = .47) G1 vs. G2: -17.4, p <0.025	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Galovski et al., 2012[6] (continued)			SF-36 social functioning G1 Pre-tx: 42.87 (4.06) G1 Post-tx: 73.87 (4.56) G2 Pre-tx: 37.45 (4.29) G2 Post-tx: 39.88 (4.69) (Hedge's g = .95) G1 vs. G2: p < .001 SF-36 emotional well-being G1 Pre-tx: 41.29 (2.77) G1 Post-tx: 66.51 (3.62) G2 Pre-tx: 40.89 (2.91) G2 Post-tx: 42.43 (3.83) (Hedge's g = 1.04) G1 vs. G2: p < .001 SF-36 general health G1 Pre-tx: 50.43 (3.38) G1 Post-tx: 64.63 (3.48) G2 Pre-tx: 50.35 (3.56) G2 Post-tx: 50.53 (3.66) (Hedge's g = .81) G1 vs. G2: p <.001		

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Gamito et al., 2010[141]	G1: Virtual reality exposure therapy "VRET" G2: CBT, exposure-based therapy (Imaginal exposure) G3: WL	BDI Mean (SD) G1 Pre-tx: 24.25 (9.46) G1 Post-tx.: 14.25 (7.67) p=0.003 SCL-90-R (Psychopathology) Depression G1 Change, p=0.011 Somatization G1 Change, p<0.01 Anxiety G1 Change, p<0.05	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Gersons et al., 2000[51]	G1: Eclectic psychotherapy (Brief Eclectic Psychotherapy) G2: WL	Symptom Checklist-90-Phobic Anxiety Subscale Mean (SD) G1 Pre-tx: 21.1 (7.3) G1 Post-tx: 13.4 (5.6) G1 3 mth FU: 13.8 (4.6) G2 Pre-tx: 22.1 (11.0) G2 Post-tx:17.8 (7.4) G2 3 mth FU: 21.1 (7.6) Post-tx G1 vs. G2, p<0.01 3-mth FU G1 vs. G2, p<0.05 Symptom Checklist-90-Anxiety Subscale Mean (SD) G1 Pre-tx: 10.1 (3.1) G1 Post-tx: 7.7 (1.6) G1 3 mth FU: 7.6 (0.9) G2 Pre-tx: 14.4 (4.7) G2 Post-tx: 9.8 (3.7) G2 3 mth FU: 9.8 (3.7) Post-tx G1 vs. G2, p<0.01 3 mth FU G1 vs. G2, p<0.05 Symptom Checklist-90-Depression Subscale Mean (SD) G1 Pre-tx: 35.1 (14.6) G1 Post-tx: 21.0 (7.4) G1 3 mth FU: 21.6 (8.5)	NR	NR	Proportions by Treatment (%, p values) Resumption of Polic work Pre-tx G1: 18% G2: 25% NS Post-tx G1: 77% G2: 70% NS 3-month Followup G1: 86% G2: 60% p<0.05

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Gersons et al., 2000[51] (continued)		G2 Pre-tx: 34.9 (13.0) G2 Post-tx: 28.5 (9.6) G2 3 mth FU: 30.5 (10.5) Post-tx G1 vs. G2, p<0.01 3 mth FU G1 vs. G2, p<0.05			
Haller et al., 2016[145]	G1: Group ICBT for depression and SUD plus CPT-M (trauma-focused CPT modified to include substance use prevention) (individual) G2: Group ICBT for depression and SUD plus ICBT for depression and SUD (individual)	PDA Mean (SD) G1 Pre-tx: 0.84 (0.26) G1 Post-tx: 0.81(0.28) G1 Post-tx (1 year followup): 0.73 (0.32) G2 Pre-tx: 0.81 (0.30) G2 Post-tx: 0.79(0.29) G1 Post-tx (1 year followup): 0.72 (0.40)	NR	NR	NR
Hamner et al., 2003[83]	G1: Risperidone 1 to 6 mg/day G2: Placebo	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Harned et al., 2014[144]	G1: DBT plus DBT PE G2: DBT	HRSD Mean (SD) G1 Pre-tx: 22.9 (5.7) G1 Post-tx: 11.8 (8.0) G1 3 month followup: 12.5 (8.2) G2 Pre-tx: 25.6 (6.2) G2 Post-tx: 15.5 (6.5) G2 3 month followup: 16.8 (3.4) Between Group Effect size, Post: 0.5, followup: 0.6 Treatment X time Interaction, F = 0.0 (1, 28), NS HRSA Mean (SD) G1 Pre-tx: 25.8 (9.0) G1 Post-tx: 14.2 (10.8) G1 3 month followup: 15.0 (10.6) G2 Pre-tx: 27.6 (10.9) G2 Post-tx: 17.8 (8.6) G2 3 month followup: 16.3 (7.0) Between Group Effect size, Post: 0.3, followup: 0.1 Treatment X time Interaction, F = 0.6 (1, 22), NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Harned et al., 2014[144] (continued)		GIS Mean (SD) G1 Pre-tx: 2.6 (0.6) G1 Post-tx: 1.1 (0.7) G1 3 month followup: 1.4 (0.9) G2 Pre-tx: 2.2 (0.7) G2 Post-tx: 1.2 (0.5) G2 3 month followup: 1.7 (0.8) Between Group Effect size, Post: 0.2, Followup: 0.2 Treatment X time Interaction, F = 0.6 (1, 16), NS			
Hien et al., 2004[57]	G1: Seeking Safety G2: Relapse prevention condition (only substance abuse) G3: UC (Non-randomized Standard community Care)	NR	NR	NR	NR
Hien et al., 2009[157] Hien et al., 2012[158]	G1: Seeking Safety G2: Psychoeducation	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Hinton et al., 2005[34]	G1: CBT-mixed (Information on PTSD and Panic Disorder, relaxation techniques, culturally appropriate visualization, cognitive restructuring, exposure to anxiety-related sensations and trauma related memories, emotional-processing protocol, and cognitive flexibility) G2: WL	Anxiety Sensitivity Index (ASI) Mean (SD) G1 Pre-tx: 3.08 (0.61) G1 2nd Assessment: 1.65 (0.45) G1 3rd Assessment: 1.86 (1.98) G1 FU Assessment: 1.98 (0.40) G2 Pre-tx: 3.27 (0.53) G2 2nd Assessment: 3.19 (0.36) G2 3rd Assessment 1.84 (0.42) G2 FU Assessment: 1.91 (0.49) Group Diffferences at 2nd Assessment, p<0.001 Group Differences at 1st, 3rd, & 4th assessments, NS Average of the Symptom Checklist-90-R's Anxiety and Depression subscale (SCL) Mean (SD) G1 Pre-tx: 2.92 (0.61) G1 2nd Assessment: 1.72 (0.43) G1 3rd Assessment: 1.77 (0.30) G1 FU Assessment: 2.02 (0.78)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Hinton et al., 2005[34] (continued)		G2 Pre-tx: 3.02 (0.51) G2 2nd Assessment: 2.94 (0.45) G2 3rd Assessment: 2.03 (0.41) G2 FU Assessment: 1.96 (0.89) Group Diffferences at 2nd Assessment, p<0.001 Group Differences at 1st, 3rd, & 4th assessments, NS			
Hinton et al., 2009[151]	G1: CBT-Mixed (Information on PTSD and Panic Disorder, muscle relaxation, guided imagery, mindfulness training, yoga-like stretching, cognitive restructuring, various exercises to teach emotional distancing and switching, and interoceptive exposure) G2: WL	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Hinton et al., 2011[152]	G1; CBT-mixed Culturally Adapted CBT (coping skills, cognitive "modification", mentions exposure) G2: Applied Muscle Relaxation	SCL Anxiety Scale Mean (SD) G1 Pre-tx: 2.5 (0.5) G1 Post-tx: 1.5 (0.7) G1 FU: 1.4 (0.6) G2 Pre-tx: 2.6 (0.6) G2 Post-tx: 2.2 (0.7) G2 FU: 2.1 (0.8) Post-tx G1 vs. G2, p<0.05 (t-test) FU G1 vs. G2, p<0.05 (t-test)	NR	NR	NR
Hogberg et al., 2007[48]	G1; EMDR G2: WL	BAI Mean (SD) Pre-tx G1 Pre-tx: 16.7 (10.0) G1 Post-tx: 9.5 (14.0) G2 Pre-tx: 13.1 (9.3) G2 Post-tx: 11.4 (4.9) Within group change G1: p<0.05 G2: NS Between group change, NS HAM-A Mean (SD) G1 Pre-tx: 16.0 (6.5) G1 Post-tx: 9.8 (7.2) G2 Pre-tx: 18.2 (6.6) G2 Post-tx: 16.1 (5.1)		GAF Mean (SD) G1 Pre-tx: 64.0 (3.6) G1 Post-tx: 78.9 (12.5) G2 Pre-tx: 64.9 (3.9) G2 Post-tx: 66.8 (6.0) Within group change G1: p<0.05 G2: NS Between group change, p<0.05 SDI Mean (SD) G1 Pre-tx: 4.5 (2.3) G1 Post-tx: 4.2 (3.3) G2 Pre-tx: 5.9 (4.5) G2 Post-tx: 5.4 (3.4)	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Hogberg et al., 2007[48] (continued)		Within group change G1: p<0.05 G2: NS Between group change, NS HAM-D Mean (SD) G1 Pre-tx: 29.5 (3.5) G1 Post-tx: 26.8 (5.0) G2 Pre-tx: 30.0 (3.4) G2 Post-tx: 31.3 (4.5) Within group change G1: NS G2: NS Between group change, p<0.05		Within group change G1: NS G2: NS Between group change, NS	
Hollifield et al., 2007[32]	G1: Acupuncture G2: CBT-mixed (Cognitive restructuring, behavior activation, and coping skills) G3: WL	Depression (HSCL-25) Mean (SD) G1 Pre-tx: 2.50 (0.70) G1 Post-tx: 1.89 (0.76) G1 3 mth FU: 1.88 (0.75) G2 Pre-tx: 2.63 (0.53) G2 Post-tx: 2.00 (0.63) G2 3 mth FU: 1.91 (0.69) G3 Pre-tx: 2.61 (0.65) G3 Post-tx: 2.53 (0.67) G3 3 mth FU: 2.53 (0.67) RMANOVA G1 vs. G2, p=0.77 G1 vs. G3, p<0.01 G2 vs. G3, p<0.01	NR	SDI Mean (SD) G1 Pre-tx: 3.78 (0.83) G1 Post-tx: 2.98 (1.26) G1 3 mth FU: 2.79 (1.32) G2 Pre-tx: 4.09 (0.81) G2 Post-tx: 3.30 (1.22) G2 3 mth FU: 3.00 (1.29) G3 Pre-tx: 4.00 (1.02) G3 Post-tx: 3.96 (1.04) G3 3 mth FU: 3.96 (1.04) G2 vs. G3, p<0.01	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Hollifield et al., 2007[32] (continued)		Anxiety (HSCL-25) Mean (SD) G1 Pre-tx: 2.45 (0.57) G1 Post-tx: 1.67 (0.72) G1 3mth FU: 1.66 (0.56) G2 Pre-tx: 2.40 (0.42) G2 Post-tx: 1.78 (0.54) G2 3 mth FU: 1.81 (0.61) G3 Pre-tx: 2.26 (0.67) G3 Post-tx: 2.14 (0.61) G3 3 mth FU: 2.14 (0.61) RMANOVA G1 vs. G2, p=0.30 G1 vs. G3, p<0.01 G2 vs. G3, p<0.01		RMANOVA G1 vs. G2, p=0.83 G1 vs. G3, p<0.01	
Ivarsson et al., 2014[24]	G1: Internet based CBT G2: Delayed treatment attention control	BDI-II (ITT) Mean (SD) G1 Pre-tx: 26.61 (11.42) G1 Post-tx: 16.11 (10.49) G2 Pre-tx: 26.35 (10.88) G2 Post-tx: 22.19 (10.50) Treatment by time interaction = -6.1 (95% CI, -10.7 to -1.6), t (58) = 2.7, p=0.009, d = 0.55 (95% CI, 0.00 to 1.09), favoring treatment BAI (ITT) Mean (SD) G1 Pre-tx: 23.03 (10.27) G1 Post-tx: 13.57 (8.15) G1 Followup 1 year: 11.95 (9.33)	QOLI (ITT) Mean (SD) G1 Pre-tx: 0.14 (1.71) G1 Post-tx: 1.15 (1.60) G2 Pre-tx: 0.59 (1.65) G2 Post-tx: 0.62 (1.93) Treatment by time interaction = 0.89 (95% CI, 0.26 to 1.51), t (55) = 2.9, P =0.006, d = 0.53 (95% CI, -0.02 to 1.06), favoring treatment	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ivarsson et al., 2014[24] (continued)		G2 Pre-tx: 22.61 (10.51) G2 Post-tx: 20.08 (10.26) Treatment by time interaction = -6.2 (95% CI, -10.3 to -2.1), t (55) = 3.0, P =0.004, d = 0.60 (95% CI, 0.04 to 1.13), favoring treatment			
Johnson et al., 2011[29]	G1: CBT-mixed (Psychoeducation and CBT restructuring) G2: UC	BDI Mean (SD) G1 Pre-tx: 24.17 (9.10) G1 Post-tx: 10.68 (8.80) G1 3 mth FU: 11.61 (10.69) G1 6 mth FU: 8.16 (8.62) G2 Pre-tx: 21.89 (11.54) G2 Post-tx: 18.53 (12.12) G2 3 mth FU: 15.73 (10.90) G2 6 mth FU: 12.85 (11.87) Time effect, p<0.0001 Treatment effect, p<0.01		NR	NR
Kearney et al., 2013[159]	G1: MBSR+TAU G2: TAU (VHA health system)	PHQ-9 Mean (SD) G1 Pre-tx: 15.92 (6) G1 Post-tx: 12 (6) G1 4 month followup: 12.39 (6) G2 Pre-tx: 16.55 (5) G2 Post-tx: 15.45 (5) G2 4 Month: 15.61 (6) Post-tx, Between group: d = -.62 (95%, CI, -1.24 to 0) 4 months, between group: d = -0.55 (95% CI, -1.18 to .08)	SF-8-MCS Mean (SD) G1 Pre-tx: 30.87 (9) G1 Post-tx: 38.27 (10) G1 4 month followup: 37.46 (10) G2 Pre-tx: 30.41 (8) G2 Post-tx: 31.4 (10) G2 4 Month: 62.17 (7) Post-tx, Between group: d = 0.69 (95% CI, 0.07 to 1.32) 4 months, Between group = d = .57 (95% CI, -.06 to 1.2)		NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Kearney et al., 2013[159] (continued)		BADS Mean (SD) G1 Pre-tx: 65.38 (20) Posttx Mindfulness: 75.33 (26) 4 month Mindfulness: 76.39 (25) Pretx TAU: 65.71 (21) Posttx TAU: 64.21 (15) 4 Month TAU: 65.68 (19) Post-tx, Between group: d = 0.52 (95% CI, -.11 to 1.15) 4 months, Between group: d = 0.47 (95% CI, -0.15 to 1.09)	Clinically meaningful change (>=10 points) at PostTx: Mindfulness: 12 (57.1%) TAU: 5 (25%) Clinically meaningful change (>=10 points) at 4months: Mindfulness: 8 (36.4%) TAU: 1 (25.6%) SF-8-PCS G1 Pre-tx: 43.43 (10) G2 Post-tx: 41.42 (10) G1 4 month followup: 43.53 (10) G2 Pre-tx: 32.02 (10) G2 Post-tx: 37.29 (11) G2 4 Month followup: 36.60 (9) Post-tx, Between group: d = 0.39 (95% CI, -0.22 to 1) 4 months, Between group: d = 0.73 (95% CI, 0.09 to 1.31		
Krakow et al., 2001[52]	G1: IRT G2: WL	NR	SF-36: no significant changes for either group (results not provided)	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Krystal et al., 2011 [85]	G1; Risperidone 1 to 4 mg/day G2: Placebo	HAMA Mean Difference (95% CI) 1.16 (-0.18 to 2.51) p=0.9 MADRS Mean Difference (95% CI) 1.19 (-.029 to 2.68) p=0.09 PANNSS Mean Difference (95% CI) -0.21 (-2.37 to 1.96) p=0.85	BLSI Mean Difference (95% CI) -0.32 (-4.04 to 3.40) p=0.87 SF-36V PCS Mean Difference (95% CI) -1.13 (-2.58 to 0.32) p=0.13 SF-36V MCS Mean Difference (95% CI) -0.26 (-2.13 to 1.61) p=0.79	NR	NR
Kubany et al., 2003[35]	G1: CBT, cognitive restructuring G2: WL	BDI G1 Mean Change from Baseline (95% CI): 70.8 p<.05 G2 Mean Change from Baseline (95% CI): 67.5 (pretherapy 1); 64.5 (pretherapy 2) p<.05	NR	NR	NR
Kubany et al., 2004[28]	G1: CBT-Mixed (Cognitive Trauma Therapy-Battered Women) G2: WL	BDI (ITT Sample) Mean (SD) G1 Pre-tx: 26.9 (10.1) G1 Post-tx: 12.0 (14.2) G2 Pre-tx: 27.4 (11.0) G2 Post-tx: 28.7 (10.5) Between group significance, NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Langkaas et al., 2017[142]	G1: PE G2: IRT	BDI-II Mean (SD) G1 Pre-tx: 25.6 (7.41) G1 Post-tx: 13.0 (10.90) G1 3 mth FU: 16.8 (9.68) G2 Pre-tx: 23.6 (7.49) G2 Post-tx: 16.4 (11.31) G2 12 mth FU: 18.0 (12.10) Treatment X Time Interaction, NS SCL-90-R GSI Mean (SD) G1 Pre-tx: 1.94 (0.50) G1 Post-tx: 0.99 (0.77) G1 3 mth FU: 1.21 (0.72) G2 Pre-tx: 1.77 (0.52) G2 Post-tx: 1.18 (0.85) G2 12 mth FU: 1.33 (0.81) Treatment X Time Interaction, NS	QOL-Psychological Mean (SD) G1 Pre-tx: 2.13 (0.52) G1 Post-tx: 3.20 (0.78) G1 3 mth FU: 2.97 (0.77) G2 Pre-tx: 2.34 (0.64) G2 Post-tx: 2.91 (0.89) G2 12 mth FU: 2.76 (0.98) Treatment X Time Interaction, p = 0.05 QOL-Social Mean (SD) G1 Pre-tx: 2.71 (0.72) G1 Post-tx: 3.28 (0.76) G1 3 mth FU: 3.15 (0.81) G2 Pre-tx: 2.82 (0.73) G2 Post-tx: 3.25 (0.75) G2 12 mth FU: 3.05 (0.83) Treatment X Time Interaction, NS	NR	NR
Li et al., 2017[172]	G1; Sertraline 135 mg G2: Placebo	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Lindauer et al., 2005[50]	G1: Eclectic psychotherapy Brief Eclectic Psychotherapy G2: WL	HADS-Depressive Subscore Mean (SD) G1 Pre-tx: 11.8 (4.3) G1 Post-tx: 8.0 (6.7) G2 Pre-tx: 9.0 (3.5) G2 Post-tx: 9.1 (5.7) G1 vs. G2, p>0.05 HADS-Anxiety Subscore Mean (SD) G1 Pre-tx: 13.1 (3.2) G1 Post-tx: 8.1 (4.8) G2 Pre-tx: 11.3 (3.3) G2 Post-tx: 12.0 (4.7) G1 vs. G2, p<0.05	NR	NR	Patients on Sick Leave (%) G1 Pre-tx: 66.7% G1 Post-tx: 33.3% G2 Pre-tx: 50% G2 Post-tx: 50% G1 vs. G2, NS

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Litz et al., 2007[33]	G1: CBT-mixed (Stress management skills, in vivo exposure, and relapse prevention) G2: Internet-delivered supportive counseling	BAI G1 Pre-tx: 18.70 (10.60) G1 Post-tx: 8.43 (5.93) G1 3mth FU: 6.11 (5.69) G1 6 mth FU: 6.38 (5.21) G2 Pre-tx: 20.92 (15.00) G2 Post-tx: 12.59 (13.45) G2 3 mth FU: 9.92 (8.19) G2 6 mth FU: 14.43 (9.96) ITT Analysis Post-tx Time effect, p<0.001 Completer Analysis 3 mth FU G1 vs. G2, NS 6 mth FU G1 vs. G2, p =0.06 BDI G1 Pre-tx: 18.87 (9.52) G1 Post-tx: 12.14 (9.56) G1 3 mth FU: 12.51 (6.53) G1 6 mth FU: 8.50 (7.54) G2 Pre-tx: 24.43 (12.08) G2 Post-tx: 17.47 (11.19) G2 3 mth FU: 13.23 (9.08) G2 6 mth FU: 16.84 (8.66)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Litz et al., 2007[33] (continued)		ITT Analysis Post-tx Time effect, p<0.001 Completer Analysis 3 mth FU G1 vs. G2, NS 6 mth FU G1 vs. G2, p<0.05			
Maguen et al., 2017[25]	G1: CBT, Impact of Killing (IOK) G2: WL	BSI Mean (SD) G1 Pre-tx: 59.6 (39.8) G1 Post-tx: 41.9 (24.9) Mean change: -17.73 (-32.87 to 2.6), t-test p = 0.0248 G2 Pre-tx: 58.7 (30.9) G2 Post-tx: 63.2 (34.6) Mean change: 4.53 (-6.65 to -15.71), t-test p = 0.3991 Between-group difference: -21.92 (-37.27 to -6.57) t-test p=, 0.16	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Markowitz et al., 2015[132] Markowitz et al., 2016[261]	G1: PE G2: IPT G3: RT	HAM-D Mean (SD) G1 Pre-tx: 20.2 (6.7) G1 Post-tx: 12.3 (8.8) Change at Post-tx: 7.3, Effect size: 1.07 G2 Pre-tx: 18.3 (6.5) G2 Post-tx: 13.8 (8.8) Change at Post-tx: 4.2, Effect size: 0.62 G3 Pre-tx: 21.0 (7.1) G3 Post-tx: 14.8 (9.1) Change at Post-tx: 7.0, Effect size: 1.03 Treatment X Time Interaction at post-tx, X^2= 0.128, p = 0.880 G1 vs. G3 Difference: -4.42, p = 0.034, Effect Size: -0.65 G2 vs. G3 Difference: -0.98, p = 0.642, Effect Size: -0.14 G2 vs. G1 Difference: 3.44, p = 0.065, Effect Size: 0.51	Quality of Life Enjoyment and Satisfaction Mean (SD) G1 Pre-tx: 43.5 (14.7) G1 Post-tx: 63.5 (19.2) Change at Post-tx: -17.9, Effect size: -1.33 G2 Pre-tx: 43.9 (15.0) G2 Post-tx: 54.6 (18.2) Change at Post-tx: -11.3, Effect size: -0.84 G3 Pre-tx: 43.1 (8.7) G3 Post-tx: 46.1 (19.2) Change at Post-tx: -0.8, Effect size: -0.06 Treatment X Time Interaction at post-tx, X^2= 3.561, p = 0.037 G1 vs. G3 Difference: 17.83, p < 0.001, Effect Size: 1.33	Social Adjustment Scale Mean (SD) G1 Pre-tx: 2.7 (0.6) G1 Post-tx: 2.1 (0.5) Change at Post-tx: 0.4, Effect size: 0.81 G2 Pre-tx: 2.7 (0.6) G2 Post-tx: 2.2 (0.5) Change at Post-tx: 0.5, Effect size: 0.93 G3 Pre-tx: 2.8 (0.4) G3 Post-tx: 2.7 (0.6) Change at Post-tx: 0.1, Effect size: 0.16 Treatment X Time Interaction at post-tx, X^2= 3.875, p = 0.022 G1 vs. G3 Difference: -0.57, p < 0.001, Effect Size: -1.05 G2 vs. G3 Difference: -0.46, p = 0.001, Effect Size: -0.83 G2 vs. G1 Difference: 0.12, p = 0.409, Effect Size: 0.21	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Markowitz et al., 2015[132] Markowitz et al., 2016[261] (continued)			G2 vs. G3 Difference: -10.13, p = 0.017, Effect Size: 0.75 G2 vs. G1 Difference: -7.69, p = 0.061, Effect Size: -0.57	Inventory of Interpersonal Problems Mean (SD) G1 Pre-tx: 1.7 (0.6) G1 Post-tx: 1.1 (0.6) Change at Post-tx: 0.7, Effect size: 1.26 G2 Pre-tx: 1.6 (0.6) G2 Post-tx: 1.0 (0.7) Change at Post-tx: 0.5, Effect size: 0.95 G3 Pre-tx: 1.5 (0.4) G3 Post-tx: 1.5 (0.6) Change at Post-tx: -0.1, Effect size: -0.19 Treatment X Time Interaction at post-tx, X2= 3.875, p = 0.022 G1 vs. G3 Difference: -0.57, p < 0.001, Effect Size: -1.05 G2 vs. G3 Difference: -0.46, p = 0.001, Effect Size: -0.83 G2 vs. G1 Difference: 0.12, p = 0.409, Effect Size: 0.21	

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Marks et al., 1998[122] Lovell et al., 2001[123]	G1: CBT, exposure-based therapy(PE) G2: CBT, cognitive restructuring G3: CBT-mixed Exposure (Combined with Cognitive Restructuring) G4: Relaxation	BDI (11 weeks) Mean Change Score (95% CI) G1: 13 (8 to 18) G2: 17 (11 to 22) G3: 18 (13 to 23) G4: 7 (3 to 11) Additional results presented in graphs BDI Mean change in G1 + G2 + G3 vs. G4 Post, p=0.004 1 mth FU, p=0.08	NR	Work/Social Adjustment (Self Report) (Completer data) Mean (SD) G1 Pre-tx: 21.5 (8.9) G1 Post-tx:11.8 (12.3) G1 1 mth FU: 9.5 (12.1) G1 3 mth FU: 5.2 (8.3) G1 6 mth FU: 4.1 (7.8) G2 Pre-tx: 26.9 (8.8) G2 Post-tx:14.3 (10.0) G2 1 mth FU:13.9 (10.9) G2 3 mth FU: 14.7 (12.1) G2 6 mth FU: 13.4 (11.7) G3 Pre-tx: 29.4 (7.9) G3 Post-tx:13.2 (12.1) G3 1 mth FU: 13.2 (12.2) G3 3 mth FU: 10.3 (9.3) G3 6 mth FU: 4.5 (6.9) G4 Pre-tx: 22.1 (9.5) G4 Post-tx:17.5 (11.6) G4 1 mth FU: 15.0 (11.3) G4 3 mth FU: 14.9 (12.3) Additional results presented in graphs Work/Social Adjustment Mean change in G1 + G2 + G3 vs. G4 Post, p=0.002 1 mth FU, p=0.006 3 mth FU, p=0.005	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Marshall et al., 2001[64]	G1: Paroxetine 20 mg/day G2: Paroxetine 40 mg/day G3: Placebo	MADRS Adjusted Mean Differences (95% CI) G1 vs. G3 -5.6 (-8.0 to -3.3) p<0.001 G2 vs. G3 -5.1 (-7.4 to -2.8) p<0.001	NR	SDS Adjusted Mean Differences (95% CI) G1 vs. G3 -2.4 (-4.1 to -0.8) p<0.005 G2 vs. G3 -2.0 (-3.7 to -0.3) p<0.001	NR
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	G1: Fluoxetine 20 to 80 mg/day G2: Placebo	MADRS Changes from Pre-tx to Post-tx Least Square Means (SE), p-value G1: -6.5 (0.45) G2: -3.5 (0.75) p<0.001 HAM-A Changes from Pre-tx to Post-tx Least Square Means (SE), p-value G1: -8.7 (0.48) G2: -5.7 (0.79) p=0.001 Hopkins 90-Item Symptom Checklist-Revised (SCL-90-R) Changes from Pre-tx to Post-tx Least Square Means (SE), p-value G1: -51.8 (4.40) G2: -36.4 (7.20) p=0.058	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Martenyi et al., 2007[62]	G1: Fluoxetine 20 mg/day G2: Fluoxetine 40 mg/day G3: Placebo	MADRS Mean change from baseline (SE) (Completer analysis) G1: -5.05 (0.82) G2: -5.04 (0.84) G3: -3.45 (1.14) p =0 .463 HAMA Mean change from baseline (SE) (Completer analysis) G1: -9.12 (0.61) G2: -9.16 (0.62) G3: -7.67 (0.84) p=.296			
Maxwell et al., 2016[124]	G1: MEST G2: CPT	BDI-II Mean (SD) G1 Pre-tx:26.13 (11.31) G1 Post-tx:20.25 (16.03) G1 3 mth FU: 18.13 (13.27) G2 Pre-tx:23.63 (16.27) G2 Post-tx:14.75 (10.99) G2 3 mth FU: 11.38 (11.08) Cohen's d = .40	NR	GAF Mean (SD) G1 Post-tx:67.25 (16.60) G2 Post-tx:69.44 (10.04) Cohen's d = -0.16	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
McDonagh et al., 2005[39]	G1: CBT-mixed (Exposure and cognitive restructuring therapy) G2: PCT G3: WL	BDI Mean (SD) G1 Pre-tx: 18.9 (9.6) G1 Post-tx: 12.9 (12.5) G2 Pre-tx: 17.0 (7.7) G2 Post-tx: 10.8 (9.5) G3 Pre-tx: 20.9 (7.8) G3 Post-tx: 19.0 (11.3) Group X Time, p>0.10 STAI Mean (SD) G1 Pre-tx: 53.5 (10.4) G1 Post-tx: 46.2 (13.9) G2 Pre-tx: 54.5 (9.2) G2 Post-tx: 46.4 (12.2) G3 Pre-tx: 54.6 (9.6) G3 Post-tx: 51.5 (9.7) Group X Time, p<0.10	QOLI Mean (SD) G1 Pre-tx: 36.1 (15.9) G1 Post-tx: 39.5 (17.0) G2 Pre-tx: 35.2 (15.3) G2 Post-tx: 39.0 (12.6) G3 Pre-tx: 36.8 (13.2) G3 Post-tx: 37.2 (14.7) Group X Time, p>0.10	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
McGovern et al., 2015[27]	G1: ICBT plus SC, manual-guided therapy focused on PTSD and substance use. G2: IAC plus SC, (focused exclusively on substance use and recovery) (arm not eligible) G3: SC (intensive out-patient program services)	Positive toxicology, n (%) G1 Pre-tx: 16 (21.9) G1 Post-tx (6 month): 10(18.5) G3 Pre-tx: 15 (20.8) G3 Post-tx (6 month):19(38.8) Difference between G1 and G3, p <0.05 Parameter Estimate and CIs for ANCOVA G1 vs. G3, 1.13 (95% CI, 0.18 to 2.08) Effect size G1 vs. G2: -0.45 ASI-Drug, Mean (SD) G1 Pre-tx: 0.13 (0.09) G1 Post-tx (6 month): 0.08(0.08) G3 Pre-tx: 0.15 (0.09) G3 Post-tx (6 month):0.09(0.09) Difference between G1 and G3, NS Parameter Estimate and CIs for ANCOVAG1 vs. G3, -0.01 (95% CI, -0.04 to 0.02) Effect size G1 vs. G2: -0.13 ASI-alcohol, Mean (SD) G1 Pre-tx: 0.21 (0.22) G1 Post-tx (6 month): 0.15 (0.19)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Mills et al., 2012[20]	G1: COPE, a modification of Concurrent Treatment of PTSD and Cocaine Dependence. (motivational enhancement, psychoeducation, in vivo exposure, imaginal exposure, and cognitive therapy) G2: TAU	BDI-II Mean (95% CI) G1 Pre-tx: 36.07 (33.17 to 38.97) G1 Post-tx: 24.44 (19.29 to 29.59) Mean difference Pre-tx to FU: -11.64 (-17.08 to -6.19), p < 0.001 G2 Pre-tx: 31.69 (28.08, 35.30) G2 Post-tx: 24.78 (20.15, 29.41) Mean difference Pre-tx to Post-tx: -6.90 (-10.84, -2.97), p < 0.001 Between group difference Pre-tx to Post-tx: -4.73 (-11.76, 2.29), NS Treatment X Time Interaction: X^2 = 1.31, p = 0.26 STAI Mean (95% CI) G1 Pre-tx: 54.69 (51.16, 58.22) G1 Post-tx: 46.44 (42.09 to 50.79) Mean difference Pre-tx to Post-tx: -8.25 (-13.64 to -2.86), p < 0.001 G2 Pre-tx: 50.42 (46.89 to 53.95) G2 Post-tx: 47.50 (43.15 to 51.85) Mean difference Pre-tx to Post-tx: -2.91 (-7.16 to 1.34), NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Mills et al., 2012[20]		Between group difference Pre-tx to post-tx: -5.34 (-12.47 to 1.80), NS Treatment X Time Interaction: X^2 = 2.69, p = 0.10 Number of Drug Classes Used Mean (95% CI) G1 Pre-tx: 3.71 (3.32 to 4.10) G1 Post-tx: 2.13 (1.68 to 2.58) Mean difference Pre-tx to Post-tx: 0.57 (0.46 to 0.72), p < 0.001 G2 Pre-tx: 3.81 (3.40 to 4.22) G2 Post-tx: 2.28 (1.71 to 2.85) Mean difference Pre-tx to post-tx: 0.60 (0.47 to 0.76), p<0.001 Between group difference Pre-tx to post-tx: 0.96(0.69, 1.34), NS Treatment X Time Interaction: X^2 = 0.10, p = 0.76 Number of Dependence Criteria Met Mean (95% CI) G1 Pre-tx: 5.33 (5.09 to 5.57) G1 Post-tx: 2.27 (1.58 to 2.96) Mean difference Pre-tx to Post-tx: 0.43 (0.31 to 0.58), p < 0.001			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Mills et al., 2012[20]		G2 Pre-tx: 5.58 (5.36 to 5.80) G2 Post-tx: 2.98 (2.27 to 3.69) Mean difference Pre-tx to post-tx: 0.52 (0.41 to 0.66), p>0.001 Between group difference Pre-tx to post-tx: 0.85 (0.60 to 1.21), NS Treatment X Time Interaction: $X^2 = 0.00$, p >0.99			
Monnelly et al., 2003[167]	G1: Risperidone 0.5 to 2.0mg/day G2: Placebo	NR	NR	NR	NR
Monson et al., 2006[1]	G1:CBT, cognitive processing therapy G2: WL	BDI Mean (SE) G1 Pre-tx: 25.39 (1.8) G1 Post-tx: 17.42 (1.6) G1 1 mth FU: 18.75 (1.9) G2 Pre-tx: 28.53 (1.6) G2 Post-tx: 27.06 (1.4) G2 1 mth FU: 23.92 (1.8) Group X Time, NS STAI Mean (SE) G1 Pre-tx: 54.38 (2.1) G1 Post-tx: 46.92 (2.1) G1 1 mth FU: 47.51 (2.4) G2 Baseline: 55.62 (1.8) G2 Postassessment: 58.16 (2.0) G2 1-month followup: 56.98 (2.3) Group X Time, p<0.01	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Monson et al., 2012[22]	G1: CBCT, manualized cognitive-behavioral conjoint therapy for PTSD delivered in a couple therapy format G2: WL	Beck Depression Mean (95% CI) G1 Pre-tx: 24.36 (19.59 to 29.12) G1 Post-tx: 12.16 (6.35 to 17.96) Change: -12.20 (-19.10 to -5.31) Effect size Hedge g: 1.16 (0.40 to 1.89) G2 Pre-tx: 22.60 (17.88 to 27.32) G2 Post-tx: 20.32 (14.79 to 25.85) Change: -2.29 (-6.37 to -1.79) Effect size Hedge g: 0.17 (-0.13 to 0.47) Change Difference Mean Between Groups: -9.91 (-17.22 to -2.60) Effect size Hedge g: 0.83 (0.10 to 1.54) Treatment X Time Interaction, t (40, 7) = -2.87, p = 0.007 State-Trait Anxiety Scale Mean (95% CI) G1 Pre-tx: 49.25 (43.67 to 54.82) G1 Post-tx: 38.65 (31.97 to 45.32) Change: -10.60 (-19.04 to -2.16) Effect size Hedge g: 0.84 (0.17 to 1.49) G2 Pre-tx: 50.90 (45.47 to 56.33) G2 Post-tx: 51.73 (45.47 to 57.99) Change: 0.84 (-4.40 to 6.08) Effect size Hedge g: -0.06 (-0.41 to 0.29) Change Difference Mean Between Groups: -11.43 (-20.55 to -2.31) Effect size Hedge g: 0.85 (0.13 to 1.57) Treatment X Time Interaction, t (44) = -2.62, p = 0.01	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Moradi et al., 2014[160]	G1: MEmory Specificity Training (MEST) G2: Control, no additional contact	BDI-II Treatment X Time Interaction, NS	NR	NR	NR
Morath et al., 2014[55]	G1: NET G2: WL	HAM-D Mean (SD) G1 Pre-tx: 22.82 (11.73) G1 Post-tx: 17.00 (9.81) G1 1 year post-tx:17.63 (9.84) G2 Pre-tx: 25.94 (6.55) G2 Post-tx: 24.18 (9.21) Treatment X Time Interaction at post-tx, F (1, 32) = 0.89, p = 0.35 SOMS Mean (SD) G1 Pre-tx: 25.12 (10.55) G1 Post-tx: 19.18 (14.93) G1 1 year post-tx:16.81 (10.00) G2 Pre-tx: 23.00 (12.75) G2 Post-tx: 26.31 (12.38) Treatment X Time Interaction at post-tx, F (1, 32) = 6.19, p = 0.02	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Mueser et al., 2008[7]	G1: CBT-mixed (CBT for PTSD) G2: UC	BDI-II Mean (SD) G1 Pre-tx: 31.48 (13.24) G1 Post-tx: 21.91 (11.52) G1 3 mth FU: 21.67 (13.32) G1 6 mth FU: 25.02 (12.85) G2 Pre-tx: 31.76 (13.76) G2 Post-tx: 27.70 (14.75) G2 3 mth FU: 30.66 (15.26) G2 6 mth FU: 31.30 (13.50) Group effect, p<0.001 BAI Mean (SD) G1 Pre-tx: 48.29 (13.04) G1 Post-tx: 42.59 (12.95) G1 3 mth FU: 41.10 (14.29) G1 6 mth FU: 43.58 (12.03) G2 Pre-tx: 49.68 (13.26) G2 Post-tx: 45.81 (14.16) G2 3 mth FU: 48.04 (15.62) G2 6 mth FU: 47.84 (13.73) Group effect, p =0.03	SF-12 - Physical Mean (SD) G1 Pre-tx: 39.81 (11.63) G1 Post-tx: 39.23 (11.26) G1 3 mth FU: 39.17 (13.61) G1 6 mth FU: 38.89 (13.44) Group effect, p=.002 G2 Pre-tx: 40.74 (11.54) G2 Post-tx: 39.34 (12.98) G2 3 mth FU: 38.14 (11.59) G2 6 mth FU: 35.81 (10.72) Group effect, p=0.002	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Mueser et al., 2008[7] (continued)		Brief Psychiatric Rating Scale Mean (SD) G1 Pre-tx: 43.92 (7.69) G1 Post-tx: 39.63 (10.00) G1 3 mth FU: 40.57 (7.33) G1 6 mth FU: 41.78 (6.81) G2 Pre-tx: 43.77 (7.42) G2 Post-tx: 42.25 (7.59) G2 3 mth FU: 43.97 (10.37) G2 6 mth FU: 46.60 (11.56) Group effect, p =0.02	SF-12-Mental Mean (SD) G1 Pre-tx:: 29.35 (9.57) G1 Post-tx: 33.81 (11.02) G1 3 mth FU: 33.92 (11.03) G1 6 mth FU: 31.19 (9.12) G2 Pre-tx: 29.37 (9.05) G2 Post-tx: 33.75 (10.93) G2 3 mth FU: 29.99 (11.44) G2 6 mth FU: 26.66 (10.01) Group effect, p=0.13		

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Nacasch et al., 2011[15]	G1: CBT, exposure-based therapy (PE) G2: TAU	BDI Mean (SD) G1 Pre-tx: 26.0 (7.9) G1 Post-tx: 13.2 (7.6) G2 Pre-tx: 31.4 (8.8) G2 Post-tx: 26.8 (10.7) Post-tx Treatment X Time, NS G1 vs. G2, p=0.007 STAI - State Mean (SD) G1 Pre-tx: 59.5 (11.6) G1 Post-tx: 44.3 (11.0) G2 Pre-tx: 60.9 (13.3) G2 Post-tx: 62.0 (12.3) Post-tx Treatment X Time, p=0.007 G1 vs. G2, p<0.001 STAI - Trait Mean (SD) G1 Pre-tx: 59.5 (8.3) G1 Post-tx: 47.7 (12.6) G2 Pre-tx: 61.0 (10.9) G2 Post-tx: 61.7 (12.5) Post-tx Treatment X Time, p=0.016 G1 vs. G2, p=0.017	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Neuner et al., 2004[161]	G1: CBT, exposure-based therapy (NET) G2: Supportive Counseling G3: Psycho-education About the nature and prevalence of PTSD	Self-Reporting Questionnaire 20 (SRQ-20) Mean (SD) G1 Pre-tx: 15.6 (2.9) G1 Post-tx: 13.1 (5.1) G1 4 mth FU: 11.9 (4.9) G1 1 year FU: 11.0 (5.1) G2 Pre-tx: 16.5 (2.7) G2 Post-tx: 14.3 (5.0) G2 4 mth FU: 12.8 (3.9) G2 1 year FU: 12.4 (4.8) G3 Pre-tx: 18.6 (2.0) G3 Post-tx: 15.3 (3.2) G3 4 mth FU: 15.1 (2.6) G3 1 year FU: 14.4 (4.1) Group X Time, NS G1 vs. G2, p<0.01 G1 vs. G3, NS	SF-12, Psychological health Scale Mean (SD) G1 Pre-tx: 0.27 (0.12) G1 Post-tx: 0.36 (0.19) G1 4 mth FU: 0.38 (0.12) G1 1 year FU: 0.44 (0.19) G2 Pre-tx: 0.34 (0.11) G2 Post-tx: 0.33 (0.21) G2 4 mth FU: 0.33 (0.14) G2 1 year FU: 0.36 (0.14) G3 Pre-tx: 0.23 (0.15) G3 Post-tx: 0.33 (0.19) G3 4 mth FU:0.37 (0.14) G3 1 year FU: 0.35 (0.17) Group X Time, NS G1 vs. G2, NS G1 vs. G3, NS		NR
Neuner et al., 2008[54]	G1: CBT, exposure based (NET) G2: Flexible Trauma Counseling G3: No-treatment monitoring group	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Neuner et al., 2010[53]	G1: CBT, exposure based (NET) G2: UC	Hopkins Symptom Checklist - 25 Depression Scale Mean (SD) G1 Pre-tx: 3.0 (0.4) G1 Post-tx: 2.6 (0.6) G2 Pre-tx: 3.0 (0.5) G2 Post-tx: 2.9 (0.5) Group X Time, NS	NR	NR	NR
Nijdam et al., 2012[154]	G1: Eclectic psychotherapy G2: EMDR	HADS - Depression Mean Estimated Differences @ first f/u: 3.58 (1.68 to 5.49) p<0.001 Mean Estimated Differences @ 2nd f/u: 1.47 (-0.44 to 3.39) p= 0.13 HADS-Anxiety Mean Estimated Differences @ 2nd f/u: 3.74 (2.03 to 5.46) p<0.001 HADS-Anxiety Mean Estimated Differences @ 2nd f/u: 0.80 (-0.93 to 2.50) p=0.36 MDD in G1 % @ baseline: 67.1 % @ 1st f/u: 36.4 % @ 2nd f/u: 19	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Nijdam et al., 2012[154] (continued)		MDD in G2 % @ baseline: 52.9 % @ 1st f/u: 13.7 % @ 2nd f/u: 14.6 MDD between group difference @ 1st f/u: p<0.05 MDD between group difference @ 2nd f/u: p=0.57 Anxiety in G1 % @ baseline: 20 % @ 1st f/u: 9.1 % @ 2nd f/u: 11.9 Anxiety in G2 % @ baseline: 11.4 % @ 1st f/u: 9.8 % @ 2nd f/u: 10.4 MDD between group difference @ 1st f/u: p=0.91 MDD between group difference @ 2nd f/u: p=0.82			
Panahi et al., 2011[71]	G1: Sertraline 50 to 200 mg/day G2: Placebo	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Petrakis et al., 2011[185]	G1: Paroxetine (40 mg/day)+ Naltrexone (50 mg/day) Participants who could not tolerate the highest dose were brought to lower doses. G2: Paroxetine (40 mg/day) +Placebo Participants who could not tolerate the highest dose were brought to lower doses. G3: Desipramine (200 mg/day) + Naltrexone (50 mg/day) Participants who could not tolerate the highest dose were brought to lower doses. G4: Desipramine (200 mg/day + Placebo Participants who could not tolerate the highest dose were brought to lower doses.	HAM-D Mean(SE) G1 Pre-tx: 13.273 (1.112) G1 Post-tx:9.328 (1.256) G2 Pre-tx: 10.950 (1.167) G2 Post-tx:8.238 (1.299) G3 Pre-tx: 11.195 (1.132) G3 Post-tx: 8.563 (1.201) G4 Pre-tx: 13.167 (1.065) G4 Post-tx: 8.943 (1.117) Time effect, p<0.00 Group X Time, NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Polusny et al., 2015[136]	G1: 8 weekly group sessions and a daylong retreat. 1st session was an orientation that included rational and psychoeducation. 7 sessions of mindfulness therapy and 1 6.5 hour retreat. G2: Group Sessions	PHQ-9 Mean (95% CI) G1 Pre-tx: 15.5 (13.9 to 17.0) G1 Post-tx: 13.6 (12.0 to 15.1) G1 2 month followup: 13.3 (11.7 to 15.0) G2 Pre-tx: 14.6 (13.1 to 16.2) G2 Post-tx: 13.9 (12.3 to 15.4) G2 2 month followup: 13.8 (12.2 to 15.4) Post-tx, Between group mean difference: 1.17 (-0.22 to 2.56), p = .1 2 month, Between group mean difference: 1.34 (-0.07 to 2.75, p=0.06 Clinically significant improvement: Posttx Mindfulness - 15 (29.4%) Posttx PCT - 11 (19.4%) 2 month Mindfullness - 13 (27.7%) 2 month PCT - 13 (22.8%) Mean difference at Posttx: 9.8%, p = .24 Mean difference at 2 months: 4.9%, p= .57	WHOQOL-BREF Mean (95% CI) G1 Pre-tx: 75.6 (71.6 to 79.7) G1 Post-tx: 80.7 (76.5 to 84.8) G1 2 month followup: 80.2 (75.9 to 84.4) G2 Pre-tx: 76.4 (72.3 to 80.4) G2 Post-tx: 78.5 (74.4 to 82.6) G2 2 month followup: 75.8 (71.7 to 79.9) Post-tx, Between group mean difference: 3.1, p = 0.08 2 month, Between group mean difference: 5.22, p=0.004	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Raskind et al., 2003[74]	G1: Prazosin 2 to 10 mg/day G2: Placebo	NR	NR	NR	NR
Raskind et al., 2007[75]	G1: Prazosin 2 to 15 mg at bedtime G2: Placebo	HAM-D Mean (SD) G1 Pre-tx: 18.3 (8.8) G1 Post-tx: 12.7 (7.7) G2 Pre-tx: 15.3 (7.8) G2 Post-tx: 14.7 (7.1) G1 vs. G2 Change, p=0.08	NR	NR	NR
Raskind et al., 2013[76]	G1: Prazosin 1 to 5 mg/day morning dose, 1 to 20mg/day bedtime dose G2: Placebo	HAM-D Adjusted Means (95% CI) G1 Pre-tx: 11.9 (9.5 to 14.3) G1 Post-tx: 10.0 (7.5 to 12.5) G2 Pre-tx: 14.7 (12.4 to 17.0) G2 Post-tx: 14.7 (12.3 to 17.1) Between Group Difference in Change from Baseline: 2.0 (-0.8 to 4.8), t = 1.39, p = 0.17	NR	NR	NR
Reger et al., 2016[18]	G1: VRE G2: PE G3: WL (minimum attention)	BDI-II Mean (SD) G1 Pre-tx: 27.87 (9.19) G1 Post-tx: 18.50 (12.70) G1 12 week: 20.04 (12.41) G1 26 week: 18.59 (11.03) G2 Pre-tx: 28.02 (11.18) G2 Post-tx: 17.06 (16.18) G2 12 week: 13.70 (13.52) G2 26 week: 14.42 (13.38) G3 Pre-tx: 27.67(9.99) G3 Post-tx: 25.63 (12.87)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Reger et al., 2016[18] (continued)		G1 vs. G3 Post-tx Differences: -7.87 (95% CI, -11.89 to -3.85), p <0.001, ES = -0.78 (95% CI, -1.18 to -0.38) G2 vs. G3 Post-tx Differences: -9.09 (95% CI, -12.97 to -5.20), p <0.001, ES = -0.90 (95% CI, -1.29 to -0.52) G1 vs. G2 Post-tx Differences: 1.22 (95% CI, -3.01 to 5.44), p = 0.714, ES = 0.12 (95% CI, -0.30 to 0.54) G1 vs. G2 12 week Differences: 4.46 (95% CI, -0.05 to 8.98), p = 0.974, ES = 0.44 (95% CI, -0.01 to 0.89) G1 vs. G2 26 week Differences: 4.63 (95% CI, -0.32 to 9.58), p = 0.967, ES = 0.46 (95% CI, -0.03 to 0.95 BAI Mean (SD) G1 Pre-tx: 24.57 (11.19) G1 Post-tx: 17.17 (12.80) G1 12 week: 19.28 (14.92) G1 26 week: 15.24 (12.19) G2 Pre-tx: 22.11 (9.34) G2 Post-tx: 13.28 (12.11) G2 12 week: 11.44 (11.79) G2 26 week: 9.83 (10.02)			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Reger et al., 2016[18] (continued)		G3 Pre-tx: 23.81 (11.09) G3 Post-tx: 18.83 (11.93) G1 vs. G3 Post-tx Differences: -5.31 (95% CI, -9.37 to -1.25), p = 0.005, ES = -0.50 (95% CI, -0.89 to -0.12) G2 vs. G3 Post-tx Differences: -5.46 (95% CI, -9.40 to -1.52), p = 0.003, ES = -0.52 (95% CI, -0.89 to -0.14) G1 vs. G2 Post-tx Differences: 0.15 (95% CI, -4.14 to 4.44), p = 0.527, ES = 0.01 (95% CI, -0.39 to 0.42) G1 vs. G2 12 week Differences: 3.51 (95% CI, -1.08 to 8.09), p = 0.933, ES = 0.33 (95% CI, -0.10 to 0.77) G1 vs. G2 26 week Differences: 3.01 (95% CI, -2.02 to 8.03), p = 0.880, ES = 0.28 (95% CI, -0.19 to 0.76			
Reich et al., 2004[84]	G1: Risperidone 0.5 to 8 mg/day G2: Placebo	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Resick et al., 2002[3] Resick et al., 2003[125]Resick et al., 2012[126]	G1: CBT, cognitive processing therapy G2: CBT, exposure-based therapy (PE) G3: WL	BDI Mean (SD) G1 Pre-tx: 23.70 (10.39) G1 Post-tx: 12.73 (11.17) G1 3 mth FU: 13.22 (11.64) G1 9 mth FU: 14.17 (11.85) G1 LTFU: 9.41 (11.13) G2 Pre-tx: 24.03 (8.88) G2 Post-tx: 16.00 (11.06) G2 3 mth FU: 16.49 (11.62) G2 9 mth FU: 16.41 (11.37) G1 LTFU: 12.06 (12.68) G3 Pre-tx: 23.33 (8.07) G3 Post-tx: 22.62 (8.59) G3 3 mth FU: 22.62 (8.59) G3 9 mth FU: 22.62 (8.59) Posttreatment differences, p<0.0001 3 mth FU differences, p<0.0001 9 mth FU differences, p<0.0001 LTFU differences, NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Resick et al., 2015[127, 128]	G1: CPT-C (Includes only the cognitive component of CPT) G2: PCT	BDI-II Mean (SE) G1 Pre-tx: 27.9 (10.2) G1 Post-tx: 19.9 (1.4) G1 6-month followup: 21.1 (1.8) G1 12-month followup: 22.7 (2.1) G2 Pre-tx: 27.9 (12.2) G2 Post-tx: 23.7 (1.4) G2 6-month followup: 24.7 (1.7) G2 12-month followup: 25.8 (2.1) Piecewise linear model for BDI-II during followup G1: .57 (.44) (.11), p =.197 G2: .22 (.42), p = .608 Difference: .35 (.60), p = .555 Between group effect sizes (d): Baseline to posttreatment: -.3 Baseline to 6 months: -.3 Baseline to 1 year: -.3	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Rothbaum et al., 1997[45]	G1: EMDR G2: WL	BDI Mean (SD) G1 Pre-tx: 21.4 (9.6) G1 Post-tx: 7.3 (5.5) G1 3 mth FU: 7.9 (5.3) G2 Pre-tx: 34.8 (13.8) G2 Post-tx: 30.4 (15.7) G1 vs. G2, p<0.05 STAI--State Mean (SD) G1 Pre-tx: 50.4 (10.6) G1 Post-tx: 31.8 (14.7) G1 3 mth FU: 37.3 (14.3) G2 Pre-tx: 63.1 (21.0) G2 Post-tx: 48.5 (15.5) STAI-Trait Mean (SD) G1 Pre-tx: 53.5 (10.9) G1 Post-tx: 35.0 (14.3) G1 3 mth FU: 37.3 (14.3) G2 Pre-tx: 64.9 (11.1) G2 Post-tx 58.8 (11.1) Post treatment G1 vs. G2, NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Rothbaum et al., 2005[13]	G1: CBT, exposure-based therapy (PE) G2: EMDR G3: WL	BDI Mean (SD) G1 Pre-tx: 16.70 (8.18) G1 Post-tx: 4.65 (4.99) G1 6 mth FU: 4.44 (5.07) G2 Pre-tx: 25.95 (7.11) G2 Post-tx: 10.70 (11.45) G2 6 mth FU: 10.53 (10.92) G3 Pre-tx: 24.05 (10.50) G3 Post-tx: 22.20 (10.55) Posttreatment G1 & G2 vs. G3, p<0.001 Posttreatment G1 vs G2, p=NS 6 mth FU G1 vs G2, p=NS STAI-State Mean (SD) G1 Pre-tx: 43.33 (12.59) G1 Post-tx: 30.00 (10.44) G1 6 mth FU: 29.19 (8.79) G2 Pre-tx: 51.10 (11.05) G2 Post-tx: 32.60 (11.62) G2 6 mth FU: 38.89 (14.54)	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Rothbaum et al., 2005[13] (continued)		G3 Pre-tx: 46.58 (13.48) G3 Post-tx: 49.00 (13.73) Posttreatment G1 & G2 vs. G3, p<0.001 Posttreatment G1 vs G2, p=NS 6 mth FU G1 vs G2, p=NS STAI-Trait G1 Pre-tx: 48.72 (8.62) G1 Post-tx: 35.56 (9.88) G1 6 mth FU: 34.19 (7.52) G2 Pre-tx: 56.80 (10.95) G2 Post-tx: 41.10 (14.48) G2 6 mth FU: 41.44 (13.26) G3 Pre-tx: 53.42 (13.07) G3 Post-tx: 53.95 (13.01) Posttreatment G1 & G2 vs. G3, p<0.001 Posttreatment G1 vs G2, p=NR 6 mth FU G1 vs. G2, NR			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Ruglass et al., 2017 [143]	G1: COPE G2: Relaspe Prevention G3: AMCG	SUI Mean (SD) G1 Pre-tx: 3.92 (2.69) G1 Post-tx: 1.60 (2.46) Change: -2.31 (95% CI, -3.23 to -1.39), p <0.001 G2 Pre-tx: 4.05 (2.35) G2 Post-tx: 0.40 (0.52) Change: -3.28 (95% -4.03 to -2.53), p <0.001 G3 Pre-tx: 3.79 (2.27) G3 Post-tx: 2.85 (2.48) Change: NR, ns Treatment X Time Interaction, p <0.001 Between group differences G1 vs G3: -0.97 (95%CI -1.72 to -0.22), p = 0.01 G2 vs G3: -2.07 (95%CI -2.92 to -1.21), p <0.001 G1 vs G2: -1.10 (95%CI -2.18 to -0.02, p =0.047	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sannibale et al. 2013[146]	G1: IT (Integrated CBT for PTSD and AUD) G2: AS, (CBT for AUD plus supportive counseling)	BDI-II G1 Pre-tx: 30.37 (13.99) G1 Post-tx: 25.13 (17.96) G1 Followup 5 months: 26.79 (18.35) G1 Followup 9 months: 23.38 (15.14) G2 Pre-tx: 28.50 (9.15) G2 Post-tx: 25.45 (12.52) G2 Followup 5 months: 25.33 (12.53) G2 Followup 9 months: 22.24 (14.82) Treatment group*time interaction ns STAI-S G1 Pre-tx: 55.89 (14.78) G1 Post-tx: 48.83 (15.90) G1 Followup 5 months: 53.17 (14.41) G1 Followup 9 months: 52.00 (14.74) G2 Pre-tx: 55.96 (10.80) G2 Post-tx: 53.64 (10.47) G2 Followup 5 months: 54.71 (14.30) G2 Followup 9 months: 49.81 (14.76) Treatment group*time interaction ns	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sannibale et al. 2013[146] (continued)		AUD diagnosis n (%) G1 Pre-tx: 33 (100) G1 Post-tx: 16 (64) G1 Followup 5 months: 10 (44) G1 Followup 9 months: 14 (52) G2 Pre-tx: 29 (100) G2 Post-tx: 12 (50) G2 Followup 5 months: 7 (33) G2 Followup 9 months: 9 (43) Treatment X time interaction ns			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sautter et al., 2015[131]	G1: SAT G2: PFE	CES-D Mean (SE) G1 Pre-tx: 31.10 (2.18) G1 Post-tx: 24.70 (2.43) G1 12-week followup: 22.13 (2.43) G2 Pre-tx: 30.21 (2.21) G2 Post-tx: 28.48 (2.45) G1 12 week followup: 28.22 (2.48) Treatment X Time Interaction at post-tx, t (79) = 1.45, p = 0.15 Treatment X Time Interaction at 12 week followup, t (79) = 2.15, p = 0.04 STAI State Mean (SE) G1 Pre-tx: 49.66 (2.37) G1 Post-tx: 39.61 (2.66) G1 12 week followup: 37.69 (2.66) G2 Pre-tx: 47.11 (2.41) G2 Post-tx: 44.58 (2.67) G1 12 week followup: 44.94 (2.71) Treatment X Time Interaction at post-tx, t (79) = 2.10, p = 0.039 Treatment X Time Interaction at 12 week followup, t (79) = 2.72, p = 0.008	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Schnurr et al., 2003[139]	G1: Exposure-based, trauma-focused group therapy (psychoeducation, cognitive restructuring, relapse prevention, and coping skills training) G2: Present-centered group Therapy(avoided trauma-focused references, cognitive restructuring, and other trauma-focused group therapy components)	NR	Only reported that there was no change on the Quality of Life Inventory. SF-36 – Mental Mean (SE) G1: Pre-tx: 30.72 (0.86) G1 7 mth FU: 31.84 (0.73) G1 12 mth FU: 30.92 (0.81) Change at 7 mths, p>0.05 Change at 12 mths, p>0.05 G2 Pre-tx: 30.54 (0.85) G2 7 mth FU: 30.75 (0.73) G2 12 mth FU: 31.83 (0.79) Change at 7 mths, p>0.05 Change at 12 mths, p>0.05 SF-36- Physical G1 Pre-tx: 41.78 (0.94) G1 7 mth FU: 40.35 (0.68) G1 12 mth FU: 40.24 (0.73)	GHQ Mean (SE) G1 Pre-tx: 32.69 (0.55) G1 7 mth FU: 31.16 (0.49) G1 12 mth FU: 31.88 (0.53) Change at 7 mths, p<0.001 Change at 12 mths, p<0.05 G2 Pre-tx: 33.45 (0.54) G2 7 mth FU: 31.62 (0.49) G2 12 mth FU: 31.19 (0.53) Change at 7 mths, p<0.01 Change at 12 mths, p<0.001 Treatment Effect, NS Treatment X Cohort, NS	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Schnurr et al., 2003[139] (continued)			Change at 7 mths, p>0.05 Change at 12 mths, p>0.05 G2 Pre-tx: 40.06 (0.95) G2 7 mth FU: 39.96 (0.68) G2 12 mth FU: 38.93 (0.71) Change at 7 mths, p>0.05 Change at 12 mths, p<0.01 Treatment Effect, NS Treatment X Cohort, NS		
Schnurr et al., 2007[138]	G1: CBT, exposure-based therapy (PE) G2: PCT	BDI Baseline Mean (95% CI) G1: 25.3 (23.8 to 26.9) G2: 23.9 (22.4 to 25.5) Least Means (95% CI) Immediate posttreatment G1: 17.4 (15.3 to 19.5) G2: 19.9 (18.0 to 21.9) p=0.04 3-month followup G1: 18.5 (16.3 to 20.7) G2: 21.1 (19.1 to 23.1) p=0.04	QOL Inventory Baseline Mean (95 % CI) G1: 0.06 (-0.24 to 0.35) G2: 0.09 (-0.26 to 0.44) Least Means (95% CI) Immediate posttreatment G1: 0.56 (0.19 to 0.93) G2: 0.24 (-0.12 to 0.60) NS	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Schnurr et al., 2007[138] (continued)		6-month followup G1: 19.2 (17.1 to 21.3) G2: 20.4 (18.2 to 22.7) NS Treatment effect, NS Treatment X Time, NS STAI Baseline Mean (95% CI) G1: 52.1 (49.9 to 54.4) G2: 52.4 (50.2 to 54.7) Least Means (95% CI) Immediate posttreatment G1: 45.7 (42.6 to 48.7) G2: 50.3 (47.4 to 53.3) p=0.01 3-month followup G1: 48.8 (45.9 to 51.8) G2: 50.5 (47.7 to 53.3) NS 6-month followup G1: 50.4 (47.3 to 53.6) G2: 50.8 (48.0 to 53.6) NS Treatment effect, NS Treatment X Time, p<0.05	3-month followup G1: 0.35 (-0.05 to 0.75) G2: 0.22 (-0.14 to 0.60) NS 6-month followup G1: 0.23 (-0.12 to 0.58) G2: 0.14 (-0.26 to 0.53) NS Treatment effect, NS Treatment X Time, NS SF-36-Mental Baseline Mean (95% CI) G1: 30.1 (28.4 to 31.7) G2: 30.6 (28.7 to 32.6) Least Means (95% CI) Immediate posttreatment G1: 37.5 (35.0 to 40.0) G2: 33.4 (30.9 to 35.8) p<0.01		

Author, Year	Intervention Groups	Comorbid I Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Schnurr et al., 2007[138] (continued)			3-month followup G1: 35.6 (33.2 to 38.1) G2: 33.8 (31.1 to 36.4) NS 6-month followup G1: 35.3 (33.0 to 37.7) G2: 33.4 (30.9 to 35.9) NS Treatment effect, NS Treatment X Time, NS SF-36-Physical Baseline Mean (95% CI) G1: 38.3 (36.4 to 40.2) G2: 39.7 (37.5 to 41.8) Least Means (95% CI) Immediate posttreatment G1: 38.1 (36.1 to 40.2) G2: 39.5 (37.5 to 41.4) NS		

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Schnurr et al., 2007[138] (continued)			3-month followup G1: 39.1 (37.1 to 41.1) G2: 38.8 (36.7 to 40.9) NS 6-month followup G1: 38.8 (36.7 to 40.8) G2: 38.3 (36.2 to 40.5) NS Treatment effect, NS Treatment X Time, NS		

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Schnyder et al., 2011[49]	G1: Eclectic psychotherapy BEP G2: WL (Minimal attention)	HADS - Anxiety Mean (SD) G1 Pre-tx:14.4 (2.6) G1 Post-tx:12.2 (4.2) G1 6 mth FU: 11.8 (5.4) G2 Pre-tx:13.8 (2.5) G2 Post-tx:13.5 (3.1) Group Effect, p<0.05 HADS - Depression G1 Pre-tx:13.4 (4.8) G1 Post-tx:10.8 (5.8) G1 6 mth FU: 11.4 (5.6) G2 Pre-tx: 10.7 (3.5) G2 Post-tx: 11.4 (4.2) Group Effect, p<0.05	NR	NR	NR
Simon et al., 2008[174]	G1: Paroxetine 12.5 to 62.5 mg/day G2: Placebo and 5 additional sessions of PE	NR	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sloan et al., 2012[17]	G1: Sertraline 25 to 200mg/day G2: Venlafaxiene 37.5 to 375mg/day Sertraline 25 to 200mg/day	NR	NR	NR	NR
Sonne et al., 2016[186]	G1: WET G2: WL	HAM-D (ITT) Mean (SE) G1 Pre-tx: 23.69 (0.55) G1 Post-tx: 22.33 (0.85) Difference: 1.36 (0.79), p =0.08, Effect size: 0.24 G2 Pre-tx: 23.69 (0.62) G2 Post-tx: 22.46 (0.89) Difference: 1.23 (0.82), p =0.13, Effect size: 0.22 Group difference for difference between pre- and post-treatment ratings:0.13 (1.14), p = 0.91, Effect size: 0.02 Group differences at follow up: Regression coefficient, B = 0.19 (95% CI, -1.94 to 2.33), Beta-coefficient = 0.01, SE = 1.09, p = 0.86	WHO-5 (ITT) Mean (SE) G1 Pre-tx: 12.73 (1.36) G1 Post-tx: 22.21 (2.67) Difference: -9.48 (2.42), p <0.01, Effect size: 0.65 G2 Pre-tx: 15.00 (1.64) G2 Post-tx: 17.75 (2.24) Difference: -2.75 (2.16), p =0.20, Effect size: 0.19 Group difference for difference between pre- and post-treatment ratings:6.73 (3.24), p = 0.04, Effect size: 0.47	SDS (ITT) Mean (SE) G1 Pre-tx: 24.65 (0.53) G1 Post-tx: 21.81 (0.88) Difference: 2.84 (0.85), p <0.01, Effect size: 0.48 G2 Pre-tx: 22.71 (0.69) G2 Post-tx: 23.20 (0.79) Difference: -0.49 (0.86), p =0.57, Effect size: 0.08 Group difference for difference between pre- and post-treatment ratings:3.32 (1.21), p < 0.01, Effect size: 0.56 Group differences at follow up: Regression coefficient, B = 2.31 (95% CI, 0.10 to 4.52), Beta-coefficient = 0.16, SE = 1.13, p = 0.04 SAS-SR(ITT) Mean (SE) G1 Pre-tx: 2.93 (0.07) G1 Post-tx: 2.68 (0.08) Difference: 0.25 (0.07), p <0.01, Effect size: 0.36	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sonne et al., 2016[186] (continued)		HAM-A (ITT) Mean (SE) G1 Pre-tx: 26.74 (0.68) G1 Post-tx: 26.41 (1.04) Difference: 0.33 (0.97), p = 0.73, Effect size: 0.05 G2 Pre-tx: 27.14 (0.72) G2 Post-tx: 26.05 (1.05) Difference: 1.09 (1.00), p =0.28, Effect size: 0.16 Group difference for difference between pre- and post-treatment ratings:-0.76 (1.39), p = 0.58, Effect size: 0.11 Group differences at follow up: Regression coefficient, B = -0.57 (95% CI, -3.19 to 2.04), Beta-coefficient = -0.03, SE = 1.34, p = 0.67	Group differences at follow up: Regression coefficient, B = -5.79 (95% CI, -12.05 to 0.46), Beta-coefficient = -0.13, SE = 3.19, p = 0.07	G2 Pre-tx: 2.96 (0.07) G2 Post-tx: 2.80 (0.08) Difference: 0.16 (0.08), p =0.04, Effect size: 0.23 Group difference for difference between pre- and post-treatment ratings: 0.09 (0.11), p = 0.39, Effect size: 0.13 Group differences at follow up: Regression coefficient, B = 0.10 (95% CI, -0.09 to 0.29), Beta-coefficient = 0.07, SE = 0.10, p = 0.29 GAF-S(ITT) Mean (SE) G1 Pre-tx: 47.43 (0.57) G1 Post-tx: 51.33 (0.93) Difference: -3.90 (0.79), p <0.01, Effect size: 0.68 G2 Pre-tx: 48.14 (0.61) G2 Post-tx: 51.82 (0.94) Difference: -3.68 (1.03), p <0.01, Effect size: 0.64 Group difference for difference between pre- and post-treatment ratings: 0.22 (1.29), p = 0.86, Effect size: 0.04	

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sonne et al., 2016[186] (continued)		HSCL-25 (ITT) Mean (SE) G1 Pre-tx: 3.03 (0.05) G1 Post-tx: 2.85 (0.07) Difference: 0.18 (0.07), p <0.01, Effect size: 0.39 G2 Pre-tx: 3.04 (0.05) G2 Post-tx: 2.94 (0.06) Difference: 0.10 (0.05), p =0.05, Effect size: 0.22 Group difference for difference between pre- and post-treatment ratings:0.08 (0.09), p = 0.37, Effect size: 0.17 Group differences at follow up: Regression coefficient, B = 0.07 (95% CI, -0.10 to 0.23), Beta-coefficient = 0.05, SE = 0.08, p = 0.42		GAF Group differences at follow up: Regression coefficient, B = 0.06 (95% CI, -2.37 to 2.48), Beta-coefficient = 0.00, SE = 1.24, p = 0.96 -F(ITT) Mean (SE) G1 Pre-tx: 48.37 (0.68) G1 Post-tx: 50.28 (0.92) Difference: -1.91 (0.79), p = 0.02, Effect size: 0.29 G2 Pre-tx: 49.04 (0.68) G2 Post-tx: 51.91 (0.96) Difference: -2.87 (0.89), p <0.01, Effect size: 0.43 Group difference for difference between pre- and post-treatment ratings: 0.96 (1.19), p = 0.42, Effect size: 0.06 Group differences at follow up: Regression coefficient, B = 1.22 (95% CI, -1.03 to 3.47), Beta-coefficient = 0.08, SE = 1.15, p = 0.29	

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Sonne et al., 2016[186] (continued)		SCL-90 (ITT) Mean (SE) G1 Pre-tx: 2.40 (0.058) G1 Post-tx: 2.35 (0.10) Difference: 0.05 (0.10), p = 0.64, Effect size: 0.06 G2 Pre-tx: 2.50 (0.08) G2 Post-tx: 2.53 (0.09) Difference: -0.03 (0.07), p =0.69, Effect size: 0.04 Group difference for difference between pre- and post-treatment ratings:0.08 (0.12), p = 0.54, Effect size: 0.10 Group differences at follow up: Regression coefficient, B = 0.12 (95% CI, -0.12 to 0.35), Beta-coefficient = 0.07, SE = 0.12, p = 0.31			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Spence et al., 2011[30]	G1: CBT-mixed (Imaginal exposure, Coping skills, Cognitive processing) G2: WL	Patient Health Questionaire-9 item G1 Pre-tx: 15.61 (4.38) G1 Post-tx: 10.17 (5.65) G1 3 mth FU: 9.91 (6.12) G2 Pre-tx: 15.05 (4.90) G2 Post-tx: 13.84 (4.95) G2 3 mth FU: NR G1 vs. G2, p<0.01 Generalized Anxiety Disorder Scale G1 Pre-tx: 12.91 (4.57) G1 Post-tx: 7.91 (5.98) G1 3 mth FU: 7.26 (5.94) G2 Pre-tx: 11.11 (3.89) G2 Post-tx: 10.63 (3.53) G2 3 mth FU: NR G1 vs. G2 @ 8 weeks: p<0.04**	NR	SDS G1 Pre-tx: 18.17 (6.96) G1 Post-tx: 13.22 (9.42) G1 3 mth FU: 11.30 (9.64) G2 Pre-tx: 19.42 (8.03) G2 Post-tx: 18.11 (6.67) G2 3 mth FU: NR G1 vs G2, p=0.07	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Stein et al., 2002[80]	G1: Olanzapine 10 to 20 mg G2: Placebo	CES -D G1: -5.25 (SD=6.27) G2: 4.88 (SD=9.66) p<.03	NR	NR	NR
Tarrier et al., 1999[129] Tarrier et al., 1999[130]	G1: CBT, exposure-based therapy G2: CBT, cognitive restructuring, Cognitive Therapy	BDI Mean (SD) G1 Pre-tx: 23.93 (10.95) G1 Post-tx: 17.43 (11.88) G1 6-mth FU: 20.41 (10.60) G2 Pre-tx: 27.45 (12.39) G2 Post-tx: 19.03 (13.20) G2 6 mth FU: 20.83 (12.79) G1 vs. G2 differences, NS 12-Month Followup G1 Pre-tx: 23.52 (10.87) G1 12 mth FU: 20.33 (11.40) G2 Pre-tx: 26.90 (12.34) G2 12 mth FU: 20.93 (13.55) G1 vs. G2 differences, NS	NR	NR	Percentage Back at Work 6 Month Followup Overall: 40% G1: 44% G2: 37%

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Tarrier et al., 1999[129] Tarrier et al., 1999[130] (continued)		BAI Mean (SD) G1 Pre-tx: 26.86 (10.75) G1 6 mth FU: 23.04 (12.18) G2 Pre-tx: 26.39 (12.05) G2 6 mth FU: 20.66 (12.97) G1 vs. G2 differences, NS 12-Month Followup G1 Pre-tx: 26.76 (10.23) G1 12 mth FU: 20.58 (13.01) G2 Pre-tx: 26.34 (12.32) G2 12 mth FU: 21.54 (14.13) G1 vs. G2 differences, NS			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Taylor et al., 2003[133]	G1: CBT, exposure-based therapy G2: EMDR G3: Relaxation Training	BDI Mean (SD) G1 Pre-tx: 26.4 (10.0) G1 Post-tx: 16.04 (9.1) G1 FU: 14.4 (11.0) G2 Pre-tx: 23.2 (7.8) G2 Post-tx: 13.0 (10.6) G2 FU: 12.7 (8.9) G3 Pre-tx: 26.3 (11.1) G3 Post-tx: 21.0 (13.8) G3 FU: 16.7 (8.9) Treatment Effects, NS Treatment X Time, NS Time Effect from Post-tx to FU, p 0.01	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
ter Heide et al., 2016[43]	G1: EMDR G2: Stabilisation	HSCL, anxiety G1 vs. G2, d = 0.09, NS HSCL, depression G1 vs. G2, d = -0.03, NS	WHOQOL-BREF, physical G1 vs. G2, d = 0.07, NS WHOQOL-BREF, psychological G1 vs. G2, d = 0.07, NS WHOQOL-BREF, social relationships G1 vs. G2, d = -0.28, NS WHOQOL-BREF, environment G1 vs. G2, d = -0.52, NS	NR	NR
Tucker et al., 2001[65]	G1: Paroxetine 20 to 50mg/day G2: Placebo	MADRS Adjusted Mean Differences (95% CI), G1 vs. G2 -3.9 (-6.4 to -1.2)	NR	SDS Adjusted Mean Differences (95% CI), G1 vs. G2 -2.6 (-4.4 to -0.7)	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Tucker et al., 2003[175] Tucker et al., 2004[176]	G1: Citalopram 20 to 50 mg/day G2: Sertraline 50 to 200 mg/day G3: Placebo	RefId 824 Systolic BP difference G1 Pre-tx: 6.66 G1 Post-tx: 0.70 G2 Pre-tx: 4.20 G2 Post-tx: -0.11 G3 Pre-tx: 7.25 G3 Post-tx: 1.00 Between group differences, NS Diastolic BP G1 Pre-tx: 2.28 G1 Post-tx: -1.65 G2 Pre-tx: 2.22 G2 Post-tx: 0.47 G3 Pre-tx: 5.60 G3 Post-tx: -2.93 Between group differences, NS	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Tucker et al., 2003[175] Tucker et al., 2004[176] (continued)		Heart rate difference Mean (SD) G1 Pre-tx: 3.22 (5.16) G1 Post-tx:1.65 (3.00) G2 Pre-tx: 2.20 (3.56) G2 Post-tx: 1.69 (3.75) G3 Pre-tx: 0.85 (1.00) G3 Post-tx: 0.57 (2.75) Between group differences, NS BDI G1 Pre-tx: 29.72(13.93) G1 Post-tx: 13.65 (11.06) G2 Pre-tx: 27.09 (12.25) G2 Post-tx: 13.67 (14.56) G3 Pre-tx: 31.60 (9.38) G3 Post-tx: 16.00 (17.21) Between group differences, p value NR			
Tucker et al., 2007[78]	G1: Topiramate 25 to 400mg/day; given 2 times a day G2: Placebo	HAM-A Mean Percentage Change (SD) G1: -53.9 (42.8) G2: -40.0 (44.2) p= 0.331 HAM-D Mean Percentage Change (SD) G1 -50.7 (45.6) G2 -33.3 (46.8) p= 0.253	Sexual Functioning Scale Mean Percentage Change (SD) G1: 2.58 (31.2) G2: 16.2 (20.4) p= 0.120	SDS Mean Percentage Change (SD) G1: -30.6 (56.4) G2: -35.4 (61.9) p=0.804	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Van Dam et al., 2013[262]	G1: SWT plus TAU G2: TAU (regular intensive treatment program for SUD based on CBT)	TLFB (days abstinent) Mean (SD) G1 Pre-tx: 19.9 (29.3) G1 Post-tx: 76.8 (15.5) G1 Followup 3 months: 61.0 (30.8) G2 Pre-tx: 20.1 (25.4) G2 Post-tx:66.0 (30.3) G2 Followup 3 months: 58.6 (38.4) Treatment X time Interaction, F(2,34) = 0.48, p = 0.620, η2 = 0.15 SUD in Remission (Primary SUD diagnosis) N (%) G1 Pre-tx: 1 (5.3) G1 Post-tx: 16.6 (87.4) G2 Pre-tx: 3 (20.0) G2 Post-tx: 10.2 (68.0) G1 vs. G2 post-tx differences NS, p's>0.23	NR	NR	NR
van den Berg et al., 2015[16]	G1: PE G2: EMDR G3: WL	NR	NR	NR	NR
van der Kolk et al., 1994[63]	G1: Fluoxetine 20 to 60mg/day G2: Placebo	HAM-D Difference in Improvement G1 vs. G2 = 7.11 ANCOVA Results F = -7.11, t = -3.72, p=0.0006	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
van der Kolk et al., 2007[47]	G1: EMDR G2: Fluoxetine 10 to 60 mg/day G3: Placebo	BDI-II Mean (SD) G1 Pre-tx: G1 Post-tx: 9.10 (6.02) G1 6 mth FU: 5.25 (5.23) G2 Pre-tx: G2 Post-tx: 13.00 (8.66) G2 6 mth FU: 14.00 (7.71) G3 Pre-tx: G3 Post-tx: 14.38 (9.74) G3: NA Treatment effect, NS Posttreatment G1 vs. G2, p= 0.08 G1 vs. G3, p=0.07 G2 vs. G3, p=0.94 Followup G1 vs. G2, p<.001	NR	NR	NR
van der Kolk et al., 2016[162]	G1: Neurofeedback G2: WL	NR	NR	IASC is available. Only subscales reported.	NR

Author, Year	Intervention Groups	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
van Emmerik et al., 2008[40]	G1: CBT-Mixed Psychoeducation, prolonged exposure, imaginal exposure, exposure in vivo, cognitive exposure G2: SWT G3: WL	BDI Mean (SD) G1 Pre-tx: 20.52 (9.43) G1 Post-tx: 15.31 (9.44) G1 FU: 14.79 (9.48) G2 Pre-tx: 22.55 (10.63) G2 Post-tx: 19.39 (13.38) G2 FU: 18.65 (13.56) G3 Pre-tx: 21.24 (8.88) G3 Post-tx: 20.66 (10.77) G3 FU: 21.17 (11.13) Group X Time Effect G1 vs G2, p=0.51 G1+G2 vs G3, p<0.04 STAI-State Mean (SD) G1 Pre-tx: 55.44 (11.22) G1 Post-tx: 46.51 (14.32) G1 FU: 46.90 (15.02) G2 Pre-tx: 54.22 (11.90) G2 Post-tx: 47.49 (15.75) G2 FU: 46.70 (15.09) G3 Pre-tx: 57.14 (11.60) G3 Post-tx: 54.06 (12.18) G3 FU: 55.08 (12.83) Group X Time Effect G1 vs. G2, p=0.81 G1+G2 vs G3, p=0.05	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
van Emmerik et al., 2008[40] (continued)		STAI-Trait G1 Pre-tx: 50.54 (8.49) G1 Post-tx: 46.23 (9.80) G1 FU: 48.15 (9.00) G2 Pre-tx: 50.35 (7.33) G2 Post-tx: 47.62 (8.81) G2 FU: 47.19 (8.76) G3 Pre-tx: 53.20 (8.70) G3 Post-tx: 52.23 (7.31) G3: 52.06 (7.28) Group X Time G1 vs G2, p=0.37 G1+G2 vs G3, p=0.20			
Wells et al., 2014[19]	G1: Metacognitive therapy G2: PE G3: WL	BDI-II Mean (SD) G1 Pre-tx: 29.9 (5.48) G1 Post-tx: 9.1 (6.79) G1 3 month followup: 12.6 (13.53) Mean difference, post-tx: 20.8 (SE, 3.48), p <0.0005, (95% CI, 12.93 to 28.67) G2 Pre-tx: 32.5 (10.06) G2 Post-tx: 17.9 (13.09) G2 3 month followup: 17.1 (14.59) Mean difference, post-tx: 14.6 (4.18), p = 0.007, (95% CI, 5.16 to 24.04) G3 Pre-tx: 40.7 (10.66) G3 Post-tx: 40 (8.68) G3 3 month followup: NA	NR	NR	NR

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Wells et al., 2014[19] (continued)		Mean difference, post-tx: 0.7 (1.56), p > 0.05, (95% CI, -2.84 to 4.24) Treatment X time interaction, post-tx: F=9.94, p = 0.001 Hedge's g: G1 Pre-Post: 1.73 G2 Pre-Post: 1.01 G1 Pre-FU: 1.01 G2 Pre-FU: 0.9 ANCOVA group effect: F = 16.53, p < 0.0005 G1 vs G3 Pre-Post: 26.09 (SE, 4.63), p < 0.0005, (95% CI, 14.26 to 37.93) G2 vs G3 Pre-Post: 18.45 (4.42), p = 0.001, (95% CI, 7.15 to 29.75) G1 vs G2 Pre-Post: 7.64 (4.15), p > 0.05, (95% CI, -2.96 to 18.25) ANCOVA group effects at followup G1 vs. G2: F = 0.39, p = 0.54 BAI Mean (SD) G1 Pre-tx: 29.5 (7.69) G1 Post-tx: 8.6 (6.06) G1 3 month followup: 12 (13.57) Mean difference, post-tx: 20.9 (SE = 2.77), p <0.0005, (95% CI, 14.64 to 27.16)			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Wells et al., 2014[19] (continued)		G2 Pre-tx: 31.5 (10.32) G2 Post-tx: 15.3 (11.89) G2 3 month followup: 13.1 (7.4) Mean difference: 16.2 (Se = 3.93), p = 0.003, (95% CI, 7.31 to 25.09) G3 Pre-tx: 36.8 (16.22) G3 Post-tx: 34.3 (15.00) G3 3 month followup: NA Mean differences, post-tx: 2.5 (SE = 1.86), (95% CI, -1.70 to 6.70) Treatment X time: F=10.33, p < 0.0005 Hedge's g: G1 Pre-Post: 2.18 G2 Pre-Post: 1.19 G1 Pre-FU: 1.09 G2 Pre-FU: 1.34 ANCOVA group effect: F = 14.63, p < 0.0005 G1 vs G3 Pre-Post: 20.88 (SE = 4), p < 0.0005, (95% CI, 10.64 to 31.11) G2 vs G3 Pre-Post: 15.5 (SE = 3.94), p = 0.002, (95% CI, 5.42 to 25.57) G1 vs G2 Pre-Post: 5.38 (3.88), p = ns, (95% CI, -15.30 to 4.54) ANCOVA group effects at followup G1 vs. G2: F = 0.04, p = 0.85			

Author, Year	Intervention Groups	Comorbid Medical Condition	QOL	Disability/Functional Impairment	Return to Work/Active Duty OR Ability to Work
Yeh et al., 2011[79]	G1: Topiramate 25 to 200mg/day G2: Placebo	BDI Mean(SD) G1 Pre-tx: 22.29 (9.47) G1 Post-tx 13.81 (10.29) G2 Pre-tx: 22.0 (11.80) G2 Post-tx:18.14 (14.77) Between Group Change, p=0.72	NR	NR	NR
Zlotnick et al., 2009[56]	G1: Seeking Safety; G2: Usual care Psychoeducational group and individual case management and drug counseling	Addicition Severity Index Mean difference (95% CI) 0.01 (-0.06 to -0.08)	NR	NR	NR
Zohar et al., 2002[72]	G1: Sertraline 50 to 200 mg/day G2: Placebo	MADRS Mean Change from Baseline (SD) G1: -9.17 (3.13) G2: -5.96 (3.33) NS	NR	NR	NR

ANOVA = analysis of variance; ANCOVA = analysis of covariance; BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CES-D = Center for Epidemiologic Studies Depression Scale; CI = confidence interval; FU = Followup; GAF = Global Assessment of Functioning; GHQ-28 = General Health Questionnaire (28 item); HADS-A =Hospital Anxiety Scale; HADS-D = Hospital Depression Scale; HAM-A = Hamilton Rating Scale for Anxiety; HAM-D = Hamilton Rating Scale for Depression; MADRS = Montgomery–Åsberg Depression Rating Scale; NR= not reported; NS = not significant; PHQ = The Patient Health Questionnaire; Pre-tx = pretreatment; Post-tx = Posttreatment; PTSD= Post-Traumatic Stress Disorder; Q-LES-Q-SF = Quality of Life Enjoyment and Satisfaction Questionnaire – Short Form; QOL = quality of life; RMANOVA, repeated measures analysis of variance; SD = standard deviation; SDS = Sheehan Disability Scale; SE = standard error; SF-36 = Short Form (36) Health Survey; SF-36V =Veterans Short Form 36 Questionnaire; STAI = State-Trait Anxiety Inventory; SUI = Substance Use Inventory.

Table F-3. Subgroup analysis of included randomized trials: reduction, remission, and loss of diagnosis

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171]	G1: Fluoxetine 10 to 60mg/day G2: Placebo	Individuals with specific PTSD symptoms	Meltzer-Brody et al., 2000[171] Symptom-Specific Effects- DTS Mean (SD) Within-Group Mean Change (Endpoint-Baseline) Intrusion Baseline G1 Baseline: 17.7 G1 Post-tx: 6.7 Change: -11.0 G2 Baseline: 21.5 G2 Post-tx: 13.5 Change: -8.0 p=0.0082 Avoidance Baseline: G1 Baseline: 9.2 G1 Post-tx: G1: 3.0 Change: -6.2 G2 Baseline: 9.3 G2 Post-tx: 6.3 Change:-3.0 p=0.0153 Numbing Baseline: G1 Baseline: 22.3 G1 Post-tx: 6.2 Change: -16.1 G2 Baseline: 22.6 G2 Post-tx: 15.1 Change: -7.5 p=0.0017	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171] (continued)			Hyperarousal Baseline: G1Baseline: 24.7 G1 Post-tx: 9.0 Change: -15.7 G2 Baseline: 26.0 G2 Post-tx: 17.3 Change: -8.7 p=0.0029 SIP Intrusion Baseline G1 Baseline: 10.1 G1 Post-tx: 2.9 Change: 7.2 G2 Baseline: 9.6 G2 Post-tx: 5.5 Change: 4.1 p=0.0108 Avoidance Baseline: G1 Baseline: 3.9 G1 Post-tx: 1.1 Change: 2.8 G2 Baseline: 4.1 G2 Post-tx: 2.5 Change: 1.6 p=0.0189		

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Connor et al., 1999[170] Meltzer-Brody et al., 2000[171] (continued)			Numbing G1 Baseline: 9.6 G2 Baseline: 10.2 Change: 7.1 G1Post-tx: 2.5 G2 Post-tx: 5.8 Change: 4.4 p=0.0028 Hyperarousal G1 Baseline: 10.5 G1 Post-tx: 3.6 Change: 6.9 G2 Baseline: 10.8 G2 Post-tx: 6.6 Change: 4.2 p=0.0118		
Davidson et al., 2001[68]	G1: Sertraline 50 to 200 mg/day G2: Placebo	Gender	CAPS-2 Treatment X Sex analysis was performed but was found to be not significant.	NR	NR
Davidson et al., 2007[166]	G1: Tiagabine 4 to16mg/day G2: Placebo	Gender Length of PTSD Diagnosis	CAPS For those with PTSD, 3 yrs: Mean Change from Baseline: G1: 39.3 (25.9), p=NR G2: 31.2 (27.9), p=NR For Women: Mean Change from Baseline: G1: 35.0 (24.8), p=NR G2: 22.4 (33.4), p=NR	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Foa et al., 1999[14] Zoellner et al., 1999[134]	G1: CBT, exposure-based therapy (PE) G2: CBT, coping skills therapy SIT G3: CBT-mixed Combined treatment (PE and SIT Training) G4: WL	Racial/ethnic minority	PSS-I, Mean (SD) African American G1 Pre-tx: 28.48 (7.82) G1 Post- tx: 14.35 (8.78) G1 12 mth FU: 13.43 (11.00) G2 Pre-tx: 35.00 (8.69) G2 Post-tx: 29.20 (8.61) G2 12 mth FU: NR Caucasian G1 Pre-tx: 30.27 (8.90) G1 Post-tx: 11.76 (8.23) G1 12 mth FU: 18.99 (12.30) G2 Pre-tx: 31.90 (4.09) G2 Post-tx: 25.80 (8.63) G2 12 mth FU: NR Main effects of treatment, p<0.001	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Friedman et al., 2007[70]	G1: Sertraline 25 to 200 mg/day G2: Placebo	Gender Substance Abuse History Severity Level	CAPS-2 Trauma type Adjusted mean Change at Endpoint (SE) Noncombat: -22.2 (4.4) Combat: -11.7 (2.4) Main Effects, p=0.039 IES Trauma Type Adjusted mean Change at Endpoint (SE) Group 1 Noncombat: -7.1 (3.7) Combat: -9.2 (2.0) Group 2 Noncombat: -18.7 (3.7) Combat: -4.4 (2.1) Gender Adjusted mean Change at Endpoint (SE) Male G1:-9.6 (2.0) G2: -6.5 (2.0) Female G1: -4.2 (4.3) G2: -16.5 (4.6) TX X Gender interaction, p<0.027 Pairwise comparisons, NS Illness severity Adjusted mean Change at Endpoint (SE): Data NR Greater change in more severely ill Main Effects, p=0.17	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Markowitz et al., 2015[132] Markowitz et al., 2016[261]	G1: PE G2: IPT G3: RT	Major Depression vs. No Major Depression Trauma Type: Sexual, Physical, Interpersonal Gender Primary Trauma Age	CAPS Major Depressive Subgroup vs.No Major Depressive Disorder Subgroup Difference between Pre-tx to post-tx did not differ significantly between groups p=ns Sexual Trauma vs. No Sexual Trauma G1 vs. G2, p = .0244 G1 vs. G3, p = 0.282 G2 vs. G3, p = 0.7742 Physical Trauma vs. No Physical Trauma G1 vs. G2, p = 0.7244 G1 vs. G3, p = 0.5670 G2 vs. G3, p = 0.5954 Interpersonal Trauma vs. No Interpersonal Trauma G1 vs. G2, p = 0.1326 G1 vs. G3, p = 0.3797 G2 vs. G3, p = 0.3886 Female vs. Male G1 vs. G2, p = 0.0355 G1 vs. G3, p = 0.2394 G2 vs. G3, p = 0.6761 Primary Trauma age≤18 vs. Primary Trauma ≥18 G1 vs. G2, p = 0.0633 G1 vs. G3, p = 0.1585 G2 vs. G3, p = 0.6217	Remission (CAPS score <20), Major Depressive Disorder Subgroup G1: 26% G2: 23% G3: 22 % Remission (CAPS score <20), No Major Depressive Disorder Subgroup Pre-tx to post-tx within group difference G1: p=0.008 G2: 0=0.032 G3: NR G1 vs. G3 Difference: p<0.05 (higher remission) G2 vs. G3 Difference: p<0.05 (higher remission)	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Marshall et al., 2001[64]	G1: Paroxetine 20 mg/day G2: Paroxetine 40 mg/day G3: Placebo	Gender Depressed vs. Nondepressed	CAPS-2 Adjusted Mean Differences (95% CI) Men G1 vs. G3: -11.7 (-23.3 to -0.1), p<0.05 G2 vs. G3:-13.4 (-24.6 to -2.2), p=0.02 Women G1 vs. G3:-13.7 (-20.4 to -6.9), p<0.001 G2 vs. G3:-11.2 (-18.0 to -4.3), p=0.002 Nondepressed G1 vs. G3:-16.8 (-23.7 to -9.8), p<0.001 G2 vs. G3:-12.7 (-19.8 to -5.6), p<0.001 Depressed G1 vs. G3: -11.0 (-20.4 to -1.7), p<0.03 G2 vs. G3: -11.8 (-20.9 to -2.7), p<0.02	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	G1: Fluoxetine 20 to 80 mg/day G2: Placebo	Gender Racial/ethnic minority Trauma Type Number of Traumas Different Symptoms Military Veterans	Martenyi et al., 2002[61] TOP-8 Changes from Pre-tx to Post-tx Least Square Mean, (SE), p - value Male G1: -9.8 (0.49) G2: -7.8 (0.77), p=0.026 Female G1: -10.8 (1.25) G2: -6.9 (2.54), p=0.169 White G1: -9.8 (0.47) G2: -7.4 (0.76) Nonwhite G1: -14.4 (1.09) G2: -18.2 (2.53), p=0.156 Combat Related Yes G1: -9.4 (0.72) G2: -5.0 (1.10), p<0.001 Combat Related No G1: -10.3 (0.65) G2: -9.6 (1.05), p=0.543 Number of Traumas, One Trauma Only G1: -9.9 (0.61) G2: -9.7 (1.00), p=0.847 Number of Traumas, ≥ 2 traumas G1: -9.9 (0.74) G2: -5.1 (1.16), p<.001	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Martenyi et al., 2002[61] Martenyi et al., 2006[173] (continued)			Dissociative Symptoms DES total score = 0 G1: -9.9 (0.69) G2: -4.4 (1.17), p<0.001 Dissociative Symptoms DES total score > 0 G1: -10.7 (0.55) G2: -9.8 (0.89), p=0.383 Martenyi et al., 2006[173] TOP-8 Mean Difference, 95% CI -3.86 (-6.12 to -1.60), p=0.001 CAPS Mean Difference, 95% CI -15.05 (-23.80 to -6.30), p<0.001 DTS Mean Difference, 95% CI -12.88 (-23.97 to -1.79), p=0.023		
Monson et al., 2006[1]	G1:CBT, CPT G2: WL	Comorbid conditions	NR	NR	Loss of PTSD Diagnosis: Endpoint: Disabled: 33% Non-disabled: 47% 1 month f/u: Disabled: 33% Non-disabled: 27%

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Mueser et al., 2008[7]	G1: CBT-mixed (CBT for PTSD) G2: UC	Severity Level	CAPS Mean (SD) Severe, CAPS > 65 G1 Pre-tx: 82.05 (14.46) G1 Post-tx: 59.68 (29.12) G1 3 mth FU: 57.23 (26.92) G1 6mth FU: 62.78 (25.01) G2 Pre-tx: 83.87 (12.45) G2 Post-tx: 79.65 (18.41) G2 3 mth FU: 74.50 (22.17) G2 6 mth FU: 74.24 (23.54) Group effect, p=0.004 Mild/Moderate, CAPS <65 G1 Pre-tx: 54.73 (4.74) G1 Post-tx: 40.71 (17.56) G1 3mth FU: 49.25 (23.77) G1 6 mth FU: 45.30 (22.73) G2 Pre-tx:56.07 (9.16) G2 Post-tx: 33.86 (15.40) G2 3 mth FU: 36.78 (25.83) G2 6 mth FU: 52.00 (21.93) Group Effect, p =.77	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
Resick et al., 2002[3] Resick et al., 2003[125] Resick et al., 2012[126]	G1: CBT, CPT G2: CBT, exposure-based therapy (PE) G3: WL	Exposed to Child Trauma	CAPS Mean (SD) No Childhood Sexual Abuse Pre-tx: 70.6 (18.9) Post-tx: 28.0 (20.7) 9 mth FU: 10.9 (9.1) Childhood Sexual Abuse Pre-tx: 76.8 (18.4) Post-tx: 28.4 (27.1) 9 mth FU: 33.3 (29.6) Time effect, p=0.000 Group effect, NS Group X Time, NS	NR	NR
Tucker et al., 2001[65]	G1: Paroxetine 20 to 50mg/day G2: Placebo	Gender	CAPS-2 Adjusted Mean Differences (95% CI), G1 vs. G2 Men:-15.15 (-24.31 to -5.98) Women: -10.00 (-18.68 to -3.30)	NR	NR

Author Year	Intervention Groups	Subgroup Analyzed	PTSD Symptom Reduction	Remission	Loss of Diagnosis
van der Kolk et al., 2007[47]	G1: EMDR G2: Fluoxetine 10 to 60 mg/day G3: Placebo	Exposure to Child Trauma	CAPS Mean (SD) Child-onset G1 Post-tx: 38.36 (20.73) G1 6 mth FU: 33.00 (22.34) G2 Post-tx: 40.20 (14.33) G2 6 mth FU: 50.43 (8.24) G3 Post-tx: 46.57 (20.18) G3 6 mth FU: NR Adult-onset: G1 Post-tx: 19.92 (14.64) G1 6 mth FU: 20.17 (19.36) G2 Post-tx: 37.75 (23.69) G2 6 mth FU:35.36 (16.76) G3 Post-tx: 31.92(13.87) G3 6 mth FU: NR Onset X Treatment Effect, NS Patients with adult-onset had greater reductions in PTSD symptoms than those with child-onset at post-tx & 6 mth; p<0.005 (ITT), p=0.02 (Completer)	Asymptomatic at Posttreatment, % Child-onset G1: 9.1 G2: 10.0 G3: 7.1 Adult-onset G1: 46.2 G2: 18.8 G3: 16.7 Asymptomatic at Followup, % Child-onset G1: 33.3 G2: 0.0 G3: NR Adult-onset G1: 75.0 G2: 0.0 G3: NR Adult-onset more likely to achieve asymptomatic end-state function in G1 only (Chi-square, ITT) Posttreatment, p=0.037 Followup, p=0.045	Lost of PTSD Diagnosis at Posttreatment, % Child-onset G1: 72.7 G2: 90.0 G3: 57.1 Adult-onset G1: 100.0 G2: 75.0 G3: 75.0 Lost of PTSD Diagnosis at Followup, % Child-onset G1: 88.9 G2: 42.9 G3: NR Adult-onset G1: 91.7 G2: 90.9 G3: NR Adult-onset more likely to lose diagnosis in G1 only (Chi-square, ITT) Posttreament, p=0.052 Followup, p=0.045 G2, adult-onset more likely to lose diagnosis than child-onset, p=0.036

CAPS = Clinician-administered PTSD Scale; CI = confidence interval; DTS = Davidson Trauma Scale; IES = Impact of Events Scale; NA = not applicable; NR= not reported; PSS-I= PTSD Symptom Scale Interview; PTSD= Post-Traumatic Stress Disorder; SD = standard deviation; SE = standard error; TOP-8 = Treatment Outcome PTSD Scale.

Table F-4. Subgroup analysis of included randomized trials: comorbidities, quality of life, and disability

Author Year	Intervention Groups	Subgroup Analyzed	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Duty
Foa et al., 1999[14] Zoellner et al., 1999[134]	G1: CBT, exposure-based therapy (PE) G2: CBT, coping skills therapy SIT G3: CBT-mixed Combined treatment (PE and SIT) G4: WL	Racial/ethnic minority	BDI, Mean (SD) African American G1 Pre-tx: 18.76 (9.66) G1 Post-tx: 7.97 (7.21) G1 12 mth FU: 9.77 (9.83) G2 Pre-tx: 29.20 (8.61) G2 Post-tx: 26.96 (16.29) G2 12 mth FU: NR Caucasian G1 Pre-tx: 20.87 (11.64) G1 Post-tx: 9.01 (8.43) G1 12 mth FU: 9.73 (11.61) G2 Pre-tx: 21.41 (10.35) G2 Post-tx: 19.40 (14.44) G2 12 mth FU: NR Main effects of treatment, p<0.001	NA	SAS-Global Mean (SD) African American G1 Pre-tx: 3.91 (1.00) G2 Pre-tx: 4.60 (1.14) G1 12 mth FU: 3.07 (1.22) G1 Post-tx: 2.74 (1.18) G2 Post-tx: 4.40 (0.89) G2 12 mth FU: NR Caucasian G1 Pre-tx: 3.80 (1.09) G1 Post-tx: 2.68 (0.94) G1 12 mth FU: 2.98 (1.47) G2 Pret-tx: 3.60 (1.07) G2 Post-tx: 3.40 (1.07) G2 12 mth FU: NR Main effects of treatment, p<0.01 No main effect for ethnicity or treatment X ethnicity	NA

Author Year	Intervention Groups	Subgroup Analyzed	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Duty
Foa et al., 1999[14] Zoellner et al., 1999[134] (continued)			STAI-State Mean (SD) African American G1 Pre-tx: 49.49 (13.41) G1 Post-tx: 33.33 (12.11) G1 12 mth FU: 35.86 (13.34) G2 Pre-tx: 62.00 (7.68) G2 Post-tx: 54.00 (14.14) G2 12 mth FU: NR Caucasian G1 Pre-tx: 51.31 (14.43) G1 Post-tx: 39.33 (13.25) G1 12 mth FU: 39.72 (14.76) G2 Pre-tx: 45.57 (10.94) G2 Post-tx: 48.60 (14.02) G2 12 mth FU: NR Main effects of treatment, $p<0.05$			

Author Year	Intervention Groups	Subgroup Analyzed	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Duty
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	G1: Fluoxetine 20 to 80 mg/day G2: Placebo	Military/Veterans	Martenyi et al., 200660 MADRS Mean Difference, 95% CI, -5.03 (-7.53 to -2.53), p<0.001 HAMA Mean Difference, 95% CI -4.70 (-7.13 to -2.27), p<0.001	Martenyi et al., 2006[173] SF-36 Mental Health Mean Difference, 95% CI, 15.20 (8.52 to 21.87), p<0.001 SF-36 Physical Functioning Mean Difference, 95% CI 0.56 (-7.43 to 8.54), p=0.891	NR	NR
Markowitz et al., 2015[132] Markowitz et al., 2016[261]	G1: PE G2: IPT G3: RT	Trauma Type: Sexual, Physical, Interpersonal Gender Primary Trauma Age	HAMD24 Sexual Trauma vs. No Sexual Trauma G1 vs. G2, p = 0.1019 G1 vs. G3, p = 0.0839 G2 vs. G3, p = 0.6254 Physical Trauma vs. No Physical Trauma G1 vs. G2, p = 0.6252 G1 vs. G3, p = 0.6074 G2 vs. G3, p = 0.4607 Interpersonal Trauma vs. No Interpersonal Trauma G1 vs. G2, p = 0.3814 G1 vs. G3, p = 0.4176 G2 vs. G3, p = 0.4947 Female vs. Male G1 vs. G2, p = 0.0964 G1 vs. G3, p = 0.4169 G2 vs. G3, p = 0.6190 Primary Trauma age<18 vs. Primary Trauma >18 G1 vs. G2, p = 0.1042 G1 vs. G3, p = 0.0634 G2 vs. G3, p = 0.6139	QLESQ Sexual Trauma vs. No Sexual Trauma G1 vs. G2, p = 0.2202 G1 vs. G3, p = 0.4399 G2 vs. G3, p = 0.3188 Physical Trauma vs. No Physical Trauma G1 vs. G2, p = 0.3362 G1 vs. G3, p = 0.1559 G2 vs. G3, p = 0.4306 Interpersonal Trauma vs. No Interpersonal Trauma G1 vs. G2, p = 0.1763 G1 vs. G3, p = 0.2589 G2 vs. G3, p = 0.3469 Female vs. Male G1 vs. G2, p = 0.5152 G1 vs. G3, p = 0.4544 G2 vs. G3, p = 0.5398 Primary Trauma age<18 vs. Primary Trauma >18 G1 vs. G2, p = 0.0905 G1 vs. G3, p = 0.3647 G2 vs. G3, p = 0.2451	SAS Sexual Trauma vs. No Sexual Trauma G1 vs. G2, p = 0.2612 G1 vs. G3, p = 0.4499 G2 vs. G3, p = 0.3740 Physical Trauma vs. No Physical Trauma G1 vs. G2, p = 0.5046 G1 vs. G3, p = 0.2857 G2 vs. G3, p = 0.4021 Interpersonal Trauma vs. No Interpersonal Trauma G1 vs. G2, p = 0.2508 G1 vs. G3, p = 0.2916 G2 vs. G3, p = 0.4814 Female vs. Male G1 vs. G2, p = 0.2956 G1 vs. G3, p = 0.0975 G2 vs. G3, p = 0.0340 Primary Trauma age<18 vs. Primary Trauma >18 G1 vs. G2, p = 0.2063 G1 vs. G3, p = 0.3233 G2 vs. G3, p = 0.5396	NR

Author Year	Intervention Groups	Subgroup Analyzed	Comorbid Condition	QOL	Disability/Functional Impairment	Return to Work/Duty
Resick et al., 2002[3] Resick et al., 2003[125] Resick et al., 2012[126]	G1: CBT, CPT G2: CBT, exposure-based therapy (PE) G3: WL	Exposure to Child Trauma	BDI Mean (SD) No Childhood Sexual Abuse Pre-tx: 22.4 (9.5) Post-tx: 10.0 (8.3) 9 mth FU: 10.9 (9.1) Childhood Sexual Abuse Pre-tx: 24.9 (9.1) Post-tx: 11.4 (10.4) 9 mth FU: 12.9 (12.7) Time effect, p=0.000 Group effect, NS Group X Time, NS	NR	NR	NR

BDI = Beck Depression Inventory; HAM-A = Hamilton Rating Scale for Anxiety; HAMD= Hamilton Rating Scale for Depression; MADRS = Montgomery–Åsberg Depression Rating Scale; NA = not applicable; NR= not reported; PTSD= Post-Traumatic Stress Disorder; QLESQ = Quality of Life, Enjoyment, and Satisfaction; QOL = quality of life; SAS = Social Adjustment Scale; SD = standard deviation; SE = standard error; SF-36 = Short Form (36) Health Survey; STAI = State-Trait Anxiety Inventory.

Table F-5. Adverse events/harms reported by included randomized controlled trials

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Akuchekian et al., 2004[77]	G1: Topiramate 25 to 500 mg/day (sensitive patients started at 12.5mg/day) G2: Placebo	NR	G1: 2 G2: 3	NR	NR	NR	NR	NR	NR	NR
Bartzokis et al., 2005[86]	G1: Risperidone 1 to 3 mg/day G2: Placebo	NR	G1: 3 G2: 2	NR	NR	NR	NR	NR	NS between groups	NS differences on Barnes Akathisia Scale, Columbia Scale, or Abnormal Involuntary Movement Scale

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Batki et al., 2014[165]	G1: Topiramate 25 to 300mg G2: Placebo	G1: 12 (85.7%) G2: 13 (81.3%) NS	NR	G1: 0 G2: 1 due to myocardial infarction (judged to be unrelated to study) NS	Suicidal ideation G1: 0 G2: 1 (hospitalized for suicidal ideation) NS	NR	NR	Sleepiness G1: 36% G2: 13% NS	NR	Loss appetite G1: 29% G2: 38% Change in sense of taste G1: 21% G2: 31% Itching G1: 21% G2: 6% Diarrhea G1: 29% G2: 19% Abnormal vision G1: 21% G2: 19% Serious AEs G1: 0 G2: 6 NS 5 of 6 SAES possibly related to study. NS

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Becker et al., 2007[183]	G1: Bupropion 100 to 300 mg/day G2: Placebo	NR	G1: 1 G2: NR	NR	NR	NR	NR	NR	NR	G1 & G2[a]: Heart pounding, concentration problems, problem achieving orgasm, & erecticle dysfunction G1:ability to achieve orgasm (positive & negative direction) & 1 reported rash G2: 30% reported increased appetite
Boden et al., 2012[58]	G1: Seeking Safety and TAU G2: TAU	NR	NR	NR	NR	NR	NR	NR	NR	no treatment-related adverse events occurred during the trial
Bohus et al., 2013[23]	G1: DBT-PTSD G2: TAU-WL	NR	NR	NR	Suicide Attempts G1: 0 (0) G2: 0 (0)	NR	NR	NR	NR	Worsening PTSD Symptoms G1: 0 (0) G2: 6 (15.8))
Brady et al., 2000[66]	G1: Sertraline 25 to 200 mg/day G2: Placebo	NR	G1: 5 G2: 5	NR	NR	Insomnia[a] G1: 16.0% G2: 4.3% p=0.01	NR	NR	Change, Mean kg G1: -1.3 G2: -0.3 p=0.01	Headache[a] G1: 20.2% G2: 28.3% Diarrhea[a] G1: 23.4% G2: 19.6% Malaise[a] G1: 17.0% G2: 15.2% Nausea[a] G1: 16.0% G2: 12.0% Drowsiness[a] G1: 12.8% G2: 9.8% Dry Mouth[a] G1: 11.7% G2: 4.3%

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Brady et al., 2005[67]	G1: Sertraline 150 mg/day G2: Placebo	NR	G1: 0 G2: 0	NR	NR	NR	NR	NR	NR	NR
Butterfield et al., 2001[82]	G1: Olanzapine 5 to 20mg/day G2: Placebo	G1: 45 G2: 3	NR	NR	NR	NR	NR	NR	G1: 6 G2: 0	Dry mouth G1: 3 G2: 0 Drowsiness G1: 3 G2: 1 Constipation G1: 3 G2: 1 Increased appetite G1: 3 G2: 0 Diarrhea G1: 2 G2: 0

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Butterfield et al., 2001[82] (cont'd)										Tingling G1: 2 G2: 0 Unsteadiness G1: 2 G2: 0 Forgetfulness G1: 3 G2: 0 Frequent urination G1: 4 G2: 1 UncomforTable D-urge to move G1: 4 G2: 0 Thirst G1: 6 G2: 0 Swelling G1: 4 G2: 0

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Carey et al., 2012[81]	G1: Olanzapine 5 to 10mg G2: Placebo	NR	G1: 1 (due to severe sedation) G2: 0	NR	NR	Insomnia G1: 3 (20%) G2: 2 (13%) p=0.564		Overall G1: 11 G2: 5 P, NR Mild G1: 5 (73%) G2: 4 (33%) p=0.014 Moderate G1: 5 G2: 1 P, NR Severe G1: 1 G2: 0 P, NR	Weight gain at 8 weeks G1: 14 (100%) G2: 5 (33%) p= 0.001 Mean G1: 5.6 (2.6) kg G2: -0.3 (3.9) kg p=0.000	Serious AEs G1: 0 G2: 0 Increased Anxiety G1: 1 (7%) G2: 2 (13%) p=0.584

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Chard et al., 2005[2]	G1: CBT, cognitive processing therapy CPT-SA G2: WL	NR	NR	NR	NR	NR	NR	NR	NR	No participants reported that their symptoms had become worse from pre- to posttreatment
Church et al., 2013[155]	G1: EFT, Emotional Freedom Techniques (brief exposure therapy combining cognitive and somatic elements, on PTSD and psychological distress symptoms in veterans) G2: WL	G1: 0 G2: 0	NR	NR	NR	NR	NR	NR	NR	No adverse events or increase in subject distress was reported.
Cloitre et al., 2010[148]	G1: CBT, exposure-based therapy(STAIR) G2: WL	NR	NR	NR	NR	NR	NR	NR	NR	CAPS, Symptom worsening posttreatment: G1: 1 (3.6) G2: 3 (7.4) G3: 5 (15) p=NS posttreatment to 6-mth fu G1: 0 (0) G2: 5 (22.7) G3: 5 (31.3) G1 vs. G2, p=0.02 G1 vs. G3, p=0.006
Cottraux, 2008[31]	G1: CBT-mixed (Exposure in imagination or in vivo and cognitive therapy) G2: Supportive Control	NR	G1: 0 G2: 5	NR	NR	NR	NR	NR	NR	Worsening of symptoms G1:0 G2: 5

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Davidson et al., 2001[68]	G1: Sertraline 50 to 200 mg/day G2: Placebo	NR	G1: 9 G2: 5	NR	NR	Insomnia G1: 35% G2: 22% p=0.04 Vivid Dreams G1: 10% G2: 4% p=0.10	NR	NR	NR	Headache G1: 33% G2: 24%, p=0.17 Diarrhea G1: 28% G2: 11%, p=0.003 Nausea G1: 23% G2: 11%, p=0.03 Drowsiness G1: 17% G2: 11%, p=0.24 Nervousness G1: 14% G2: 8%, p=0.27 Fatigue G1: 13% G2: 5%, p=0.05 Decreased Appetite G1: 12% G2: 1%, p=0.001 Dry Mouth G1: 10% G2: 7%, p=0.45
Davidson et al., 2003[184]	G1: Mirtazapine 15 to 45 mg/day G2: Placebo	G1: 3 G2: 3	G1: 3 G2: 3	NR	NR	NR	NR	NR	G1: 3 G2: 1	Palpitations G1: 0 G2: 3 (33.3%) Increased appetite: G1: 6 (35.3%) G2: 1 (11.1%)

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Davidson et al., 2006[69]	G1: Venlafaxine 75 to 300mg/day G2: Sertraline 50 to 200mg/day G3: Placebo	NR	G1: 17, 9.5% G2: 22, 12.7% G3: 19, 10.6%	None related to study med	NR	Insomnia[a] G1: 24, 13% G2: 18, 10% G3: 16, 9%	NR	Fatigue[a] G1: 19, 11% G2: 24, 14% G3: 17, 9% Somnolence[a] G1: 21, 12% G2: 18, 10% G3: 24, 13%	Kg[a] G1 -.5 G2: -.3 G3: +.9 G1 vs G3: p=0.00064 G2 vs G3: p=0.0242	Headache[a] G1: 53, 29% G2: 57, 32% G3: 55, 29% Nausea[a] G1 45, 24% G2: 39, 23% G3: 27, 14% Diarrhea[a] G1: 22, 12% G2: 47, 26% G3: 25, 13% Dry Mouth[a] G1: 34, 18% G2: 26, 15% G3: 27, 15% Dizziness[a] G1: 24, 13% G2: 21, 10% G3: 14, 8% Constipation[a] G1: 21, 12% G2: 12, 7% G3: 18, 10% Appetite Decrease[a] G1: 21, 12% G2: 13, 8% G3: 11, 6%

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Davidson et al., 2006[73]	G1: Venlafaxine 37.5 to 300 mg/day G2: Placebo	NR	G1: 15 G2: 9	NR	NR	G1: 12 G2: 17	NR	Somnolence G1: 9 G2: 9	Weight Change of 7% or greater G1: 20 G2: 12	Reported by at Least 5% of patients Headache G1: 46 G2: 44 Nausea G1: 35 G2: 19 Dizziness G1: 29 G2: 19 Dry Mouth G1: 21 G2: 8 Constipation G1: 20 G2: 5 Fatigue G1: 13 G2: 6 Insomnia G1: 12 G2: 17 Decreased libido G1: 8 G2: 6 Nasopharyngitis G1: 8 G2: 11 Increased Sweating G1: 21 G2: 6

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Davidson et al., 2007[166]	G1: Tiagabine 4 to16mg/day G2: Placebo	G1: NR G2: NR	G1: 8% G2: 8%	NR	NR	NR	NR	Somno-lence G1: 20% G2: 10%	NR	Vomiting G1: 11 G2: 4 Tremor G1: 10 G2: 6 Dizziness G1: 32% G2: 13% Headache G1: 25% G2: 27% Nausea G1: 18% G2: 20% Serious Adverse Event G1:1 G2:0 One individual experienced dizziness, loss of consciousness, and nausea

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Davis et al., 2008[164]	G1: Divalproex 1000 to 3000 mg/day G2: Placebo	NR (reported AEs greater than 6% in each group)	G1: 3 G2: 1	NR	NR	NR	NR	G1: 12 G2: <6	NR	SAE unrelated to study G1: 1 G2: 0 Lack of Efficacy: G1:0 G2:1 Dizziness: G1: 24 G2: <6 Nausea: G1: 14 G2: <6 GI tract upset: G1: 12 G2: <6 Diarrhea: G1: 12 G2: <6 Increased urinary frequency: G1: 10 G2: <6 Headache: G1: 10 G2: <6 Memory Deficit: G1: 10 G2: <6 Abnormal vision: G1: 7 G2: <6

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Davis et al., 2008[164] (cont'd)										Muscle weakness/myalgia: G1: <6 G2: 7
Ehlers et al., 2014[9]	G1: Intensive CT (standard CT over a much shorter period) G2: Standard CT G3: Supportive Therapy G4: WL	G1:0 (0%) G2:0 (0%) G3:0 (0%) G4:0 (0%)	NR	NR	NR	NR	NR	NR	NR	No AEs' were reported in any group (i.e., negative reactions to treatment procedures). Symptom Deterioration(CAPS), n(%) G1:0 (0) G2:1(3.2) G3: 3 (10.0) G4: 6 (20.0) G1 and G2 did not significantly differ from G3
Foa et al., 2005[12]	G1: CBT, exposure-based therapy(PE) G2: CBT-mixed (PE plus CR) G3: WL	NR	Overall: 12	Overall: 1	Overall: 4	NR	NR	NR	NR	NR
Forbes et al., 2012[4]	G1: CBT, CPT G2: TAU	NA	NA	NA	NA	NA	NA	NA	NA	no treatment-related adverse events occurred during the trial

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Ford et al., 2011[59]	G1: Trauma Affect Regulation: Guide for Education and Therapy (TARGET) G2: PCT G3: WL	NA	NA	NA	NA	NA	NA	NA	NA	no treatment-related adverse events occurred during the trial Worsening of symptoms: 3 of G1 and 1 of G2 showed evidence of symptom worsening at post-tx; by 6 months all improved from baseline. From post-tx to 3 month FU: 4 G1 and 3 G1 reported worsened PTSD symptoms; all but two improved at 6-months. From post-tx to 6 month FU 0 G2 and 3 G1 reported worsened PTSD symptoms.
Ford et al., 2013[60]	G1: Trauma Affect Regulation: Guide for Education and Therapy (TARGET), G2: SGT	NR	NR	NR	NR	NR	NR	NR	NR	No instances of serious adverse events involving clinically significant deterioration that required crisis care or intensive treatment. Symptom Worsen (CAPS $\geq$7 points higher than at baseline) G1: 4 (11%) G2: 6 (18%) Between group differences NS

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Friedman et al., 2007[70]	G1: Sertraline 25 to 200 mg/day G2: Placebo	G1: NR G2: NR	G1: 11 G2: 5	NR	NR	Insomnia[a] G1: 12 G2: 8	NR	Fatigue[a] G1: 9 G2: 1 Somnolence[a] G1: 12 G2: 7	NR	Diarrhea[a] G1: 27 G2: 15 Headache[a] G1: 23 G2: 20 Nausea[a] G1: 18 G2: 8
Galovski et al., 2012[6]	G1: Modified CBT. (potential addition of stressor sessions and variable treatment length) G2: Delayed treatment symptom monitoring	G1: 0 (0%) G1: 0 (0%)	NR	NR	NR	NR	NR	NR	NR	Reported no adverse events
Hamner et al., 2003[83]	G1: Risperidone 1 to 6 mg/day G2: Placebo	NR	G1: 0 G2: 0	NR	NR	NR	NR	NR	NR	Akathisia, n G1: 1 G2: 0 Nausea and vomiting, n G1: 1 G2: 0

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Harned et al., 2014[144]	G1: DBT plus DBT PE G2: DBT	NR	NR	NR	Committed G1: 0 (0) G2: 1 (11.1) Rate of any Suicide Attempt (ITT) G1: 37.5% G2: 50.0% Abstinent from Suicidal Behavior during followup G1: 91.7% G2: 100%	NR	NR	NR	NR	Any NSSI (ITT) G1: 68.8% G2: 87.5% Abstinent from NSSI during followup G1: 75% G2: 66.7%
Hien et al., 2004[57]	G1: Seeking Safety G2: Relapse prevention condition (only substance abuse) G3: Usual care (Non-randomized Standard community Care)	NR	NR	NR	NR	NR	NR	NR	NR	Psychiatric Hospitalization G1: 5% G2: 5% G3: 6%
Hien et al., 2009[157] Hien et al., 2012[158]	G1: Seeking Safety G2: Psychoeducation	NR	NR	NR	NR	NR	NR	NR	NR	no increase in either treatment-as-usual dropout or adverse events

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Hogberg et al., 2007[48]	G1; EMDR G2: WL	NR	G1: 1[b] G2: 0	NR	NR	NR	NR	NR	NR	NR
Hollifield et al., 2007[32]	G1: Acupuncture G2: CBT-mixed (Cognitive restructuring, behavior activation, and coping skills) G3: WL	NR	G1: 1 G2: 0 G3: NR	NR	NR	NR	NR	NR	NR	Perceived kidney pain G1: 1 G2: 0 G3:0
Ivarsson et al., 2014[24]	G1: Internet based CBT G2: Delayed treatment attention control	NR	NR	NR	NR	NR	NR	NR	NR	Symptom Deterioration (IES-R) G1:1 (3.2) G2:0 (0%) Symptom Deterioration (CGI-I) G1: 2 (6.1) G2: 8 (25.8)
Johnson et al., 2011[29]	G1: CBT-mixed (Psychoeducation and CBT restructuring) G2: Usual care	NR	G1: 0 G2: 0	NR	NR	NR	NR	NR	NR	7 hospitalizations (5 medical, 2 substance related) and 4 life-threatening traumatic experiences (2 abuse-related) reported over the course of the 6-month followup period.
Kearney et al., 2013[159]	G1: MBSR+TAU G2: TAU (VHA health system)	G1: 0 (0%) G2: 0 (0%)	NR	NR	NR	NR	NR	NR	NR	NR
Krakow et al., 2001[52]	G1: IRT G2: WL	NR	G1: 4 G2: NR	NR	NR	NR	NR	NR	NR	4 patients reported increased negative imagery and eventually withdrew, and 12 of 66 who completed treatment did not complete followup for unknown reasons.

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Langkaas et al., 2017[142]	G1: PE G2: IRT	NR	NR	NR	NR	NR	NR	NR	NR	Deteriorated G1 Post-tx: 0% G2 Post-tx: 3% G1 12 mth FU:3% G2 12 mth FU: 9%
Li et al., 2017[172]	G1; Sertraline 135 mg G2: Placebo	NR	G1: 2 G2: 1	NR	NR	Insomnia G1: 10 G2: 7	NR	Drowsiness G1: 9 G2: 5	NR	Nausea[a] G1: 12 (33.3) G2: 8 (8 (22.2) Headache[a] G1: 11 (30.6) G2: 6 (16.7) Diarrhea[a] G1: 5 (13.9) G2: 2 (5.6) Dry Mouth[a] G1: 8 (22.2) G2: 5 (13.9) Asthesnia[a] G1: 7 (19.4) G2: 4 (11.1) Constipation[a] G1: 7 (19.4) G2: 3 (11.1) Decreased appetite[a] G1:6 (16.7) G2: 2 (5.6) Diarrhea[a] G1: 5 (13.9) G2: 2 (5.6)

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Krystal et al., 2011[85]	G1; Risperidone 1 to 4 mg/day G2: Placebo	Overall: 206 G1: 109 G2: 97 p= 0.08 (Coded using Medical Dictionary for Regulatory Activities)	G1: 1 G2: 1	NR	NR	NR	NR	Somnolence Overall: 15 G1: 13 G2: 2 p= 0.00 Fatigue Overall: 18 G1: 18 G2: 0 p=0.00	Overall: 23 G1: 20 G2: 3 p= 0.00	Disturbance in attention Overall: 11 G1: 9 G2: 2 p=0.03 Gastrointestinal disorders Overall: 78 G1: 41 G2: 37 p=0.59 Salivary hypersecretion Overall: 14 G1: 13 G2: 1 p=0.00 Psychiatric disorders Overall:65 G1: 42 G2: 23 p=0.01 Decreased Libido Overall: 8 G1:8 G2:0 p=0.00 General disorders and administration site conditions: Overall: 49 G1: 31 G2: 18 p=0.04

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Krystal et al., 2011[85] (cont'd)										Respiratory, thoracic and mediastinal disorders Overall:24 G1: 20 G2: 4 p=0.00 Dyspnea Overall G1: 8 G2: 0 p=0.00 Nasal congestion G1: 6 G2: 0 p=0.01
Markowitz et al., 2015[132] Markowitz et al., 2016[261]	G1: PE G2: IPT G3: RT	NR	NR	NR	NR	NR	NR	NR	NR	Worsening Depression G1: 0 G2: 0 G3: 2
Marshall et al., 2001[64]	G1: Paroxetine 20 mg/day G2: Paroxetine 40 mg/day G3: Placebo	NR	G1: 21 G2: 28 G3: 18	NR	NR	NR	NR	NR	NR	Serious Adverse Events G1 & G2: 9 combined G3: 0 The study reports that the most commonly reported AEs associated with paroxetine use (with an incidence of at least 10% and twice that of placebo) were asthenia, diarrhea, abnormal ejaculation, impotence, nausea, and somnolence (data NR)."

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Martenyi et al., 2002[61] Martenyi et al., 2006[173]	G1: Fluoxetine 20 to 80 mg/day G2: Placebo	Martenyi et al., 2002[61] G1: 53% G2: 55% Martenyi et al., 2006[173] G1: 55.5% G2: 55.9%	Martenyi et al., 2002[61] G1: 2.7% G2: 4.0% Martenyi et al., 2006[173] G1: 3 G2: 1	NR	NR	Martenyi et al., 2002[61] Insomnia G1: 12% G2: 12% Martenyi et al., 2006[173] Insomnia G1: 14.5% G2: 11.8%	NR	NR	NR	Martenyi et al., 2002[61] Most Commonly Reported Headache G1: 16% G2: 15% Nausea G1: 14% G2: 7% Dry Mouth G1: 7% G2: 7% Anxiety G1: G2: 7% Martenyi et al., 2006[173] Most Commonly Reported (>5%) Headache G1: 15.5% G2: 11.8% Nausea G1: 12.7% G2: 5.9% Vomiting G1: 6.4% G2: 2.9% Dry Mouth: G1: 7.3% G2: 11.8% Abdominal Pain G1: 7.3% G2: 2.9% Diarrhea G1: 5.5% G2: 2.9 % Nervousness: G1: 5.5% G2: 0.0%

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Martenyi et al., 2007[62]	G1: Fluoxetine 20 mg/day G2: Fluoxetine 40 mg/day G3: Placebo	G1: 68% G2: 78% G3: 65%	G1: 4.3% G2: 13.1% G3: 8.0%	G1: 0 G2: 0 G3: 0	G1: 1 G2: 3 G3: 0	NR	NR	NR	NR	Serious Adverse Events, n G1: 1 (thoughts of self-mutilation) G2: 5 (2 patients' anxiety; 1 patient, chest pain; 1 patient, suicidal ideation; and 1 patient, gastritis) G3: 2 (palpitation, thyroid carcinoma).
McGovern et al., 2015[27]	G1: ICBT plus SC, manual-guided therapy focused on PTSD and substance use. G2: IAC plus SC, (focused exclusively on substance use and recovery) (arm not eligible) G3: SC (intensive out-patient program services)	G1: 0 (0) G2: 0 (0)	NR	NR	NR	NR	NR	NR	NR	NR
Mills et al., 2012[20]	G1: COPE, a modification of Concurrent Treatment of PTSD and Cocaine Dependence. (motivational enhancement, psychoeducation, in vivo exposure, imaginal exposure, and cognitive therapy) G2: TAU.	NR	NR	G1: 1 (2%, but patient had a preexisting medical condition) G2: 0 (0%)	G1: 2 (4%) G2: 5 (10%)	NR	NR	NR	NR	NR

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Monnelly et al., 2003[167]	G1: Risperidone 0.5 to 2.0mg/day G2: Placebo	G1: 4 G2: 3	G1: 1 G2: 0	NR	NR	NR	NR	NR	NR	Urinary retention G1:1 G2:0 Mild Adverse Events G1: 4 G2: 2.
Monson et al., 2006[1]	G1: CBT, cognitive processing therapy G2: WL	NR	NR	NR	NR	NR	NR	NR	NR	no serious adverse events in either condition
Monson et al., 2012[22]	G1: CBCT, manualized cognitive-behavioral conjoint therapy for PTSD delivered in a couple therapy format G2: WL	NR	G1: 1 (severe intimate aggression) G2: 0	NR	NR	NR	NR	NR	NR	Serious Adverse Event G1: 1 (severe intimate aggression) G2: 0
Mueser et al., 2008[7]	G1: CBT-mixed (CBT for PTSD) G2: Usual care	NR	G1: 2 withdrawals due to "other psychiatric symptoms" G2: NR	NR	NR	NR	NR	NR	NR	NR
Neuner et al., 2010[53]	G1: CBT, exposure based (NET) G2: UC	NR	NR	NR	G1: 2 G2: 0	NR	NR	NR	NR	NR

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Panahi et al., 2011[71]	G1: Sertraline 50 to 200 mg/day G2: Placebo	NR	NR	NR	NR	Insomnia G1: 10 G2: 4	NR	Drowsiness G1: 5 G2: 2	NR	AE reported by at least 10% Headache G1: 10 G2: 6 Nausea G1: 10 G2: 5 Restlessness G1: 8 G2: 5 Diarrhea G1: 7 G2: 4 Dry Mouth G1: 6 G2: 5 Asthenia G1: 5 G2: 2 Decreased appetite G1: 5 G2: 3 Constipation G1: 5 G2: 3 Decreased libido G1: 4 G2: 2

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Petrakis et al., 2012[185]	G1: Paroxetine (40 mg/day) + Naltrexone (50 mg/day) Participants who could not tolerate the highest dose were brought to lower doses. G2: Paroxetine (40 mg/day) +Placebo Participants who could not tolerate the highest dose were brought to lower doses. G3: Desipramine (200 mg/day) + Naltrexone (50 mg/day) Participants who could not tolerate the highest dose were brought to lower doses. G4: Desipramine (200 mg/day + Placebo Participants who could not tolerate the highest dose were brought to lower doses.	G1: 2 G2: 3 G3: 1 G4: 3	G1: 0 G2: 0 G3: 2 G4: 0	NR	NR	NR	NR	NR	NR	Adverse Effects of Desipramine (G3 or G4) Dizziness or lightheaded: 2 Tachycardia: 1 Adverse Effects of Paroxetine (G2 only) Experienced a Seizure: 1 Side Effects of Desipramine: reported significantly more gastrointestinal symptoms (abdominal pain, nausea, vomiting, loss of appetite, constipation, diarrhea, dry mouth, coughing up blood, vomiting, black/blood/light stool, yellow eyes, weight gain, and increased thirst than paroxetine treated subjects (F = 7.67, p=0.007)
Raskind et al., 2003[74]	G1: Prazosin 2 to 10 mg/day G2: Placebo	none serious	NR	NR	NR	NR	NR	NR	NR	Serious Adverse Events G1: 0 G2:0 Mild Orthostatic Hypotension, n G1: 2 (resolved upon dose increase) G2: 0

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Raskind et al., 2007[75]	G1: Prazosin 2 to 15 mg at bedtime G2: Placebo	NR	G1: 3 G2: 1	NR	NR	Insomnia G1: 1 G2: 1	NR	NR	NR	Dizziness G1: 9 G2: 6 Nasal or sinus Congestion G1: 6 G2:1 Headache G1: 3 G2: 1 Dry Mouth G1: 2 G2:0 Sweating G1: 0 G2:1 Depression G1: 0 G2: 1 Lower extremity edema G1: 0 G2: 1 Blood Pressure: No significant difference
Raskind et al., 2013[76]	G1: Prazosin 1 to 5 mg/day morning dose, 1 to 20mg/day bedtime dose G2: Placebo	Treatment Related G1: 20 G2: 18 Miscella-neous G1: 16 (50%) G2: 23 (66%)	G1: 2 G2: 0NR	NR	G1: 0 G2: 2 (1 participant hospital-lized for suicidal ideation; 1 suicide attempt)	NR	NR	Drowsiness G1: 1 G2: 3	NR	Depression G1: 0 G2: 2 Lack of Energy G1: 0 G2: 1
Reger et al., 2016[18]	G1: VRE G2: PE G3: WL	NR	Increase in symptom-atology G1: 3 (6%) G2: 1 (2%) G3: 1 (2%)	NR	NR	NR	NR	NR	NR	NR

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Reich et al., 2004[84]	G1: Risperidone 0.5 to 8 mg/day G2: Placebo	G1: 4 G2: 1	G1: 1 G2: 0	NR	NR	NR	NR	NR	Mean Increase in Weight G1: 2.5 lb G2: 3lb	Reported by Each Group G1: Sedation, dry mouth, tremor, apathy, and poor concentration G2: Sedation # or % not reported for specific adverse events
Resick et al., 2002[3] Resick et al., 2003[125] Resick et al., 2012[126]	G1: CBT, cognitive processing therapy G2: CBT, exposure-based therapy (PE) G3: WL	NR	NR	NR	NR	NR	NR	NR	NR	no adverse events associated with the followup assessments. Over time period participants had experienced many adverse events, but none were attributed to the therapy they had received years before or to the LTFU assessment itself.
Resick et al., 2015[127, 128]	G1: CPT-C (only cognitive component) G2: PCT	During treatment: G1: 20 (38%) G2: 21 (42%) During treatment related to study procedures: G1: 10 (19%) G2: 3 (6%) During followup: G1: 13 (24.7%) G2: 15 (30%)	NR	NR	Ideation During treatment: G1: 2 (3.8%) G2: 3 (6%) F[1, 613] = .21, p = .647) Ideation During followup: G1: 1 (1.9%) G2: 2 (4%) p=ns Suicide attempt during follow up. G1: 1 (1.9%) G2: 0 (0%)	NR	NR	NR	NR	Increased PTSD During treatment: G1: 11 (20.9%) G2: 6 (12%) Increased PTSD During followup: G1: 1 (1.9%) G2: 1 (2%)

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Sannibale et al. 2013[146]	G1: IT (Integrated CBT for PTSD and AUD) G2: AS, (CBT for AUD plus SC)	G1: 1 (3.0) G2: 1 (3.4)	NR	NR	NR	NR	NR	NR	NR	NR
Schnurr et al., 2003[139]	G1: Exposure-based, trauma-focused group therapy G2: Present-centered group Therapy	NR	NR	G1: 0 G2: 4 One death in G2 was suicide. The other 3 deaths in the G2 group were of "natural causes"	NR	NR	NR	NR	NR	NR
Schnurr et al., 2007[138]	G1: CBT, exposure-based therapy (PE) G2: PCT	G1: 5 G2: 14	G1: NR G2: NR	G1: 0 G2: 2 (non-suicide)	G1: 1 G2: 3	NR	NR	NR	NR	Psychiatric hospitalization G1: 4 G2: 9
Simon et al., 2008[174]	G1: Paroxetine 12.5 to 62.5 mg/day G2: Placebo Placebo and 5 additional sessions of prolonged exposure	G1: All reported at least 1 G2: All reported at least 1	G1: 1 G2: 1	NR	G1: 1 G2: 0	G1: 89% G2: 85%	NR	NR	NR	Concentration and Memory Difficulties G1: 89% G2: 85% Drowsiness G1: 67% G2: 77%

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Sonne et al., 2016[186]	G1: WET G2: WL	NR	10 overall G1:NR G2: NR	NR	NR	NR	NR	NR	NR	NR
Stein et al., 2002[80]	G1: Olanzapine 10 to 20 mg G2: Placebo	G1: 3 G2: 2	G1: 3 G2: 2	G1: 0 G2: 0	G1: 0 G2: 0	G1: 0 G2: 0	G1: 0 G2: 0	G1: 2 G2: 0	G1: 13 lbs. mean weight gain G2: NR	G1: 0 G2: 0
Taylor et al., 2003[133]	G1: CBT, exposure-based therapy G2: EMDR G3: Relaxation Training	NR	NR	NR	NR	NR	NR	NR	NR	NR
ter Heide et al., 2016[43]	G1: EMDR G2: Stabilisation	NR	G1: 0 (0%) G2: 1 (2%) (symptom increase)	NR	NR	NR	NR	NR	NR	CAPS Severity change Deterioration (≥-10 points) G1: 7/32 (21.9) G2:8/31 (25.8)
Tucker et al., 2001[65]	G1: Paroxetine 20 to 50mg/day G2: Placebo	NR	G1: 17.97 (11.9%) G2: 10 (6.4%)	NR	NR	NR	NR	Somnolence G1: 17.2% G2: 3.8%	NR	Nausea G1: 19.2% G2: 8.3% Dry Mouth G1: 13.9% G2: 4.5% Asthenia G1: 13.2% G2: 5.8% Abnormal-ejaculation G1: 11.8% G2: 3.7% Incidence of non-ejaculation-related sexual adverse events (decreased libido, impotence, female genital disorders) G1: 7.3% G2: 2.6%

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Tucker et al., 2003[175] Tucker et al., 2004[176]		Overall NR (just specific)	2 overall; group not specified	NR	NR	Insomnia G1: 13 G2: 6 G3: 6	NR	Fatigue G1: 8 G2: 6 G3: 3	NR	Jitteriness G1: 6 G2: 6 G3: 2 GI distress G1: 3 G2: 6 G3: 2 Nausea G1: 5 G2: 8 G3: 3 Vomiting G1: 1 G2: 1 G3: 0 Decreased appetite G1: 9 G2: 8 G3: 1 Increased appetite G1: 7 G2: 8 G3: 5 Decreased sexual function G1: 4 G2: 1 G3: 0 Dizziness G1: 4 G2: 4 G3: 2 Sweating, chills G1: 3 G2: 4 G3: 0

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Tucker et al., 2007[78]	G1: Topiramate 25 to 400mg/day; given 2 times a day G2: Placebo	G1: 45[c] G2: 25[c]	G1: 4 G2: 3	NR	NR	G1: 4 G2: 3	Nervousness G1: 4 G2: 1	Fatigue G1: 4 G2: 0	Weight gain in each condition G1: -1.8 (3.3 kgs G2: -1.1 (2.6) kgs p=0.434	Headache G1: 7 G2: 5 Sinusitis G1: 5 G2: 2 Taste Perversion G1: 5 G2: 0 Language problems G1: 4 G2: 3 Dyspepsia G1: 4 G2: 2 Paresthesia G1: 4 G2: 1 Hypertension G1: 2 G2: 4 Difficulty with concentration/attention G1:2 G2: 4

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
van den Berg et al., 2015[16]	G1: PE G2: EMDR G3: WL	NR	NR	NR	NR	NR	NR	NR	NR	Serious AEs (none judged to be related to the study) G1: 2 (4%) G2: 1 (2%) G3: 4 (8%)
van der Kolk et al., 1994[63]	G1: Fluoxetine 20 to 60mg/day G2: Placebo	NR	NR	NR	NR	NR	NR	NR	NR	Side Effects Reported at p<0.05 level Diarrhea, n G1: 25 G2: 16 Sweating, n G1: 20 G2: 10 Headaches, n G1: 10 G2: 3
van Emmerik et al., 2008[40]	G1: CBT-Mixed Psychoeducation, prolonged exposure, imaginal exposure, exposure in vivo, cognitive exposure G2: SWT G3: WL	NR	NR	NR	NR	NR	NR	NR	NR	NR

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Yeh et al., 2011[79]	G1: Topiramate 25 to 200mg/day G2: Placebo	NR	G1: 1 G2: 0	NR	NR	NR	NR	Somnolence G1: 23% G2: 35%	NR	Insomnia G1: 23% G2: 7% Paresthia G1: 17% Headache G1: 11% G2: 21% Irritability G1: 11% Dyspepsia G1: 17% Difficulty with Concentration G1: 11%

Author Year	Intervention Groups	Overall AE	Withdrawal Due to AE	Mortality	Suicidality	Disturbed Sleep	Agitation	Sedation	Weight Gain	Other Adverse Effects
Zohar et al., 2002[72]	G1: Sertraline 50 to 200 mg/day G2: Placebo	>10% overall	G1: 3 G2: 1	NR	NR	NR	NR	NR	NR	Nausea G1: 8 G2: 4 Headache G1: 6 G2: 3 Drowsiness G1: 6 G2: 3 Asthenia G1: 4 G2: 1 Increased appetite G1: 3 G2: 2 Dry mouth G1: 3 G2: 2 Decreased appetite G1: 3 G2: 1

[a] Reported by at least 10 percent of patients
[b] Adverse event was an adverse reaction during the provocation and somatic investigation using SPECT.
[c] Number of adverse events occurring in > 20 percent of subjects.
Abbreviations: AE = adverse events; kg = kilogram; NA = not applicable; NR= not reported; NS = not significant; SAE = serious adverse events.
EPC: Should this be “harms”?

Appendix G. Documentation of Trials Rated High Risk of Bias

Overview of This Appendix

As explained in the Methods and Results chapters of the main report on posttraumatic stress disorder (PTSD), we did not include in our main analyses any trials that originally met our eligibility criteria but were rated high risk of bias. Our focus was solely on trials of either low or medium risk of bias. In some cases, however, these high risk-of- bias trials offered some additional information about our conclusions for efficacy or comparative effectiveness.

Reasons for rating trials as high risk of bias included problems that could relate to randomization and allocation concealment, similarity of compared groups at baseline, masking of patients and study personnel, use of intent-to-treat analysis, or overall and differential loss to followup. In general terms, these trials had flaws or were underpowered to show statistically significant differences. In some cases, significant (or nonsignificant) differences had very small effect sizes. Appendix E provides additional information and rationale for our risk-of-bias assessments. We had no trials rated high risk of bias for adverse events or harms.

Psychotherapy Trials

This appendix provides information on trial findings about psychotherapies (Key Question [KQ] 1) in the same basic order as the psychological interventions covered in the Results chapter – namely, cognitive behavioral interventions of all types, eye movement desensitization and reprocessing (EMDR), and other psychotherapies. Several of these various trials did have findings consistent with those reported in the main systematic review.

Tables in this appendix describe the trials. Entries are in alphabetical order by last name of the first author of the article(s) in question. For duration of treatment (or trial), in some cases the investigators reported only the number of sessions, rather than the length of the treatment or the trial (in, e.g., weeks or months). Some trials measured certain outcomes at some point, such as 3 months, after treatment ended (usually referred to as posttreatment). Disease severity was measured frequently by the Clinician-Administered PTSD Scale (CAPS); these are the data reported in the tables unless another instrument, such as the Davidson Trauma Scale or the PTSD Checklist, is specified. Severity measures can be reported as mean scores or a range of mean scores across groups for the CAPS or another PTSD measure listed. As in the main report, inactive arms for these trials included waitlist or usual care (which included treatment as usual as well).

Pharmacologic Trials

We also present information on the high risk-of-bias trials of pharmacological interventions (KQ 2). These include a wide array of antidepressants, anticonvulsants (or mood stabilizers), and antipsychotics, among other pharmacologic agents. As with psychological interventions, we report on both efficacy trials (placebo controls) and on comparative effectiveness (from head-to-head trials – i.e., active comparators). Several of these various trials did have findings consistent with those reported in the main systematic review.

Tables in this appendix describe the trials using the organization previously described.

Efficacy or Comparative Effectiveness of Psychological Interventions (Key Question 1)

Cognitive Behavioral Therapy

Several trials addressed a wide array of cognitive behavioral therapies (CBT). These included cognitive interventions, coping skills interventions, exposure treatments of various types, and interventions with "mixed" CBT components, including various combinations of psychoeducation, self-monitoring, stress management, relaxation training, skills training, exposure (imaginal, or in vivo, or both), cognitive restructuring, guided imagery, mindfulness training, breathing retraining, crisis/safety planning, and relapse prevention.

Three separate trials tested three cognitive interventions: two tested cognitive processing therapy (CPT) and one tested web-based cognitive therapy (CT) (see Table G-1). For the CPT trial with person-centered therapy (PCT) as the comparator, we considered PCT to be an active comparator but not one for which we were interested in examining the comparative effectiveness with interventions of interest. For the other CPT trail and the CT trial, both provided findings consistent with those from the trials described in the main report on all outcomes.

Table G-1. Characteristics of cognitive intervention trials omitted from main analyses because of high risk of bias

Trial	Arm Dose (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female; % Nonwhite
Butollo et al., 2015[204]	DET (74) CPT (74) (only 67 analyzed)	24 sessions (6 months)	Type I Trauma Mixed	IES-R 66 to 67	36	66 NR
Knaevelsrud et al., 2015[224]	Web-based CT (79) Waitlist (80)	5 weeks (3 months)	War-related Mixed	PDS 30.35 to 30.65	28	72 NR
Suris et al., 2013[253]	Randomized: CPT (72) PCT (57) Analyzed: CPT (52) PCT (34)	12 weeks (1 week, 2 months, 4 months, 6 months)	Military sexual trauma	82 to 85	46	85 66

CAPS = Clinician-Administered PTSD Scale; CPT = cognitive processing therapy; CT, cognitive therapy; PCT = patient-centered therapy; PDS = Posttraumatic Diagnostic Scale; F = female; N = total number randomized/assigned to intervention and control groups; PTSD = posttraumatic stress disorder; y = year.

We rated three trials of CBT- coping skills as high risk of bias (Table G-2). One trial compared stress inoculation training (SIT) with narrative exposure therapy (NET); another compared SIT with a waitlist group. The third trial tested an affect management intervention versus waitlist. Treatment-related improvements in reducing PTSD symptoms at posttreatment were reported for SIT versus waitlist only. These findings are consistent with the single trials of these interventions included in our qualitative synthesis.

Table G-2. Characteristics of coping skills trials omitted from main analyses because of high risk of bias

Trial	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Foa et al., 1991[210]	SIT (17) PE (14) SC (14) Waitlist (10)	9 weeks (none)	Female Assault	Interviewer severity rating 24.4 to 25.8	32	100 27
Hensel-Dittman et al., 2011[216]	NET (15) SIT (13)	4 weeks (6 and 12 months)	Male and female Experienced organized violence	85.2 to 96.5	NR	NR NR
Zlotnick et al., 1997[259]	Affect management (17) Waitlist (16)	15 weeks (none)	Female Childhood sexual abuse	DTS 66.9 to 74.7	39	100 3

CBT = cognitive behavioral therapy; CBT Cope = cognitive behavioral therapy-coping skills; CBT-M = cognitive behavioral therapy mixed; DTS = Davidson Trauma Scale; F = female; IES-R = Impact of Events Scale – Revised; N = total number randomized/assigned to intervention and control groups; NET = narrative exposure therapy; NR = not reported; PCL = PTSD Checklist; PE = prolonged exposure; PTSD = posttraumatic stress disorder; relax = relaxation; SC = supportive counseling; SIT = stress inoculation training; y = year.

We rated 17 trials of CBT - exposure interventions (see Table G-3). The types of "exposure" therapies differed appreciably across these trials. Like the included studies, a majority of the high risk-of-bias trials of exposure found that the CBT-exposure group did significantly better than the inactive comparator group, especially with respect to reducing PTSD symptoms (using any of the available symptom measures), achieving remission, and losing the PTSD diagnosis. Persons in the exposure interventions also tended to do better as well in reducing depression symptoms. Although these findings were similar to those from the low or medium risk-of-bias trials, precision was lower, with wider confidence intervals. Similar to the set of included trials, few high risk-of-bias trials examined anxiety symptoms, functional status, quality of life, and functional impairment outcomes; when they did, however, findings were similar to those of included studies.

Table G-3. Characteristics of exposure trials omitted from main analyses because of high risk of bias

Study	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Ahmadizadeh et al., 2013[198]	Exposure (25) Problem solving (25) Combined (25) Control (25)	15 sessions (3 months)	Combat related	NR	42	NR NR
Arntz et al., 2007[199]	CBT-exposure (42) CBT-exposure (29) Cross-over (17)	10 weeks (1 month)	Mixed	PSS-SR 25.0 to 29.4	35	66 28
Beidel et al., 2011[201]	CBT-M (18) Exposure (17)	17 weeks (none)	Male Combat	84.9 to 90.6	59	0 0
Brom et al., 1989[203]	Desen (31) Hypno (29) Psychoeducation (29)	15 sessions (3 months)	Netherlands Mixed	IES 46.3 to 50.8	42	79 NR
Butollo et al., 2015[204]	DET (74) CPT (74) (only 67 analyzed)	24 sessions (6 months)	Type I Trauma Mixed	IES-R 66 to 67	36	66 NR
Feske et al., 2008[209]	PE (11) Usual care (13)	6 months	NR	PDS-I 34.9 to 35.2	43	100 95
Foa et al., 1991[210]	SIT (17) PE (14) SC (14) Waitlist (10)	9 weeks	Female Sexual abuse, assault	Interviewer severity rating 24.4 to 25.78	32	100 27
Franklin et al., 2017[211]	PE via iPhone (10) PE via computer (7) TAU (8)	10 sessions (1 month)	Veterans	61.1 to 74.3	46	7 30
Ghafoori et al., 2017[214]	PE (47) PCT (24)	12 weeks	Male and Female Complex Trauma	53.5 to 61.2	35	83 72
Ironson et al., 2002[219]	EMDR (10) PE (12)	6 weeks (3 months)	Domestic violence/child sexual abuse	PSS-SR 26.6 to 34.6	NR	77 NR
Johnson et al., 2006[221]	Randomized (Total: 51)[a] PE (Unclear) CM (Unclear) EMDR (Unclear) Waitlist (14)	Mean number of weekly sessions[c] PE: 9.66 EMDR: 6.33 WL: 5.89 (3 months)	Female Mixed	61.8 to 82.0	39	100 17
Keane et al., 1989[223]	Flooding (11) Waitlist (13)	14 to 16 sessions[b] (6 months)	Male Combat	PTSD Symptom Checklist 36.4 to 36.5	35	0 21
McLay et al., 2011[232]	VR-exposure (10) Usual care (10)	10 weeks	Active duty service members	82.8 to 83.5	24	5 NR
Paunovic et al., 2001[239]	Exposure (10) CBT-M (10)	16 to 20 weeks (6 months)	Male and female Refugees	95.1 to 98.4	38	15 NR
Rauch et al., 2015[245]	PE (18) PCT (18)	10-12 sessions	Military veterans	77 to 79	32	8 17

Study	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Ready et al., 2010[246]	VR (6) PCT (5)	10 sessions (6 months)	Male Combat	93.8	58	0 46
Vera et al., 2011[255]	PE (7) UC (7)	15 sessions	Spanish Speaking Puerto Ricans Mixed	53 to 73	46	0 100

[a] The number of participants randomized to each active treatment group was not reported. A total of 27 participants from the active treatment groups were analyzed, 9 in each treatment group.

CBT-M = cognitive behavioral therapy mixed; CAPS = Clinician-Administered PTSD Scale for DSM-IV; CPT = cognitive processing therapy; CM = Counting Method; CR = cognitive restructuring; desen = desensitization; DET = dialogical exposure therapy; EMDR = eye movement desensitization and reprocessing; F = female; f/u = followup; hypno = hypnotherapy; IES = Impact of Event Scale; IES-R = Impact of Event Scale – revised; NR = not reported; PCT = present-centered therapy (a type of supportive therapy); PE = prolonged exposure; PSS = PTSD symptom scale;; relax = relaxation; SC = supportive control; SIT = stress inoculation training; y = year.

Fifteen trials tested a considerable array of "mixed" CBT interventions (Table G-4). Generally, their findings were consistent with those from low or medium risk-of-bias trials on all the outcomes examined. Specifically, a majority of the high risk-of-bias studies found that the CBT- mixed group had significantly better results than did those in the various comparison groups; these included reducing PTSD symptoms, achieving remission, and losing the PTSD diagnosis, as well as reducing depression symptoms. Similar to the set of included study evidence, few of these omitted trials examined anxiety symptoms, substance use, functional status, quality of life or functional impairment outcomes; when they reported such findings, however, they were similar to those from included studies.

Table G-4. Characteristics of mixed intervention trials omitted from main analyses because of high risk of bias

Trial	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female % Nonwhite
Beck et al., 2009[200]	CBT-M (17) MCC (16)	14 weeks (3 months)	Male and female MVA	57.3 to 57.8	43	82 11
Beidel et al., 2011[201]	CBT-M (18) Exposure (17)	17 weeks	Male Combat	84.9 to 90.6	59	0 0
Difede et al., 2007[206]	CBT-M (15) Usual care (16)	12 weeks (12 to 13 weeks)	Disaster workers World Trade Center attack	50.5 to 51.7	46	3 23
Dorrepaal et al., 2012[207]	CBT-M ("Stabilitizing group treatment") (38) Usual care (33)	20 weeks (post)	Complex PTSD and severe comorbidity	DTS 80 to 90	39	NR NR
Dunne et al., 2012[208]	TF-CBT (13) Waitlist (13)	10 weeks (post)	MVC-related PTSD (specifically WAD)	PDS 21 to 23	32	50 NR
Echeburua et al., 1996[263]	CBT-M (10) CBT Cope (10)	5 weeks (1, 3, 6, and 12 months)	Female Sexual assault	NR	22	100 NR

Trial	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female % Nonwhite
Lee et al., 2002[227]	EMDR (12) CBT-M[b] (SIT+PE) (12)	7 weeks (3 months)	Male and female Mixed	IES 55.3	35	46 NR
Littleton et al., 2016[229]	Interactive online therapist-facilitated CBT (46) Psychoeducation self-help website (41)	14 weeks (post, 3 months)	Rape related PTSD	PSS-I 23 to 23.7	22	100 47
Mueser et al., 2015[234]	CBT for PTSD (104) Brief treatment (97)	12 to 16 weeks (post, 6 months, 12 months)	PTSD and severe mental illness	85.76 to 86.06	44	69 66
Margolies et al., 2013[231]	CBTI plus IRT (20) Waitlist (20)	4 sessions over 6 weeks (post collected 2 weeks after 6 week treatment period)	Combat Veterans	PSS-SR 39.8 to 41.8	38	10 60
Paunovic et al., 2001[239]	Exposure (10) CBT-M (10)	16 to 20 weeks (6 months)	Male and female Refugees	95.1 to 98.4	38	15 NR
Polak et al., 2015[247]	TF-CBT plus breathing biofeedback (4) TF-CBT (4)	5 to 18 sessions (post)	Chronic PTSD Mixed	IES-R 41.5 to 45	45	75 NR
Power et al., 2002[243]	EMDR (39) CBT-M[a] (Exp+CR) (37) Waitlist (29)	10 weeks	Male and female Mixed	IES 32.6 to 35.1	39	42 NR
Stecker et al., 2014[251]	Brief CBT (123) Usual care (151)	1 session (1 month, 3 months, 6 months)	Veterans of Iraq war with PTSD	PTSD Checklist 59.2 to 59.7	29	13 31
Ulmer et al., 2011[254]	CBT-M (12) Usual care (9)	6 biweekly sessions, over 12 weeks	Male and female Recently deployed veterans	PCL-M 63.1 to 63.4	46	31.8 66.6

[a] The information provided after CBT-M indicates the content of the mixed intervention (see abbreviations below).

CBT Cope = cognitive behavioral therapy-coping skills; CBT-M = cognitive behavioral therapy-mixed; CR = cognitive restructuring; EMDR = eye movement desensitization and reprocessing; exp = exposure therapy; IES = Impact of Event Scale; MCC = minimum contact comparison group; NR = not reported; PCL-M = PTSD Checklist-Military Version; PE = prolonged exposure; relax = relaxation; SIT = stress inoculation training; y = year.

Eye Movement Desensitization and Reprocessing

Seven trials of eye movement desensitization and reprocessing (EMDR) were rated high risk of bias (see Table G-5). These seven trials had findings consistent with those from included trials on various outcomes. Like the trials rated either low or medium risk of bias, a majority of the high risk-of-bias studies found that the EMDR group had significantly better outcomes than patients in an inactive comparator group in terms of reducing PTSD symptoms, losing the PTSD diagnosis, and reducing depression. Few of these seven trials examined any other coexisting condition, functional status, quality of life, or disability or functional impairments.

Table G-5. Characteristics of studies of eye movement desensitization and reprocessing omitted from main analyses because of high risk of bias

Trial	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Ironson et al., 2002[219]	EMDR (10) PE (12)	6 weeks (3 months)	Domestic violence Childhood sexual abuse	PSS-SR 26.6 to 34.6	NR	77 NR
Johnson et al., 2006[221]	Randomized (Total: 51)[a] PE (Unclear) CM (Unclear) EMDR (Unclear) Waitlist (14)	Mean number of weekly sessions PE: 9.66 EMDR: 6.33 Waitlist: 5.89 (3 months)	Female Mixed	61.8 to 82.0	39	100 17
Karatzias et al., 2011[222]	EMDR (23) EFT (23)	8 weeks (3 months)	Male and female Mixed	70.7 to 66.1	40	57 NR
Lee et al., 2002[227]	EMDR (12) SITPE (12)	7 weeks (3 months)	Australian male and female Mixed	IES 55.3	35	46 NR
Marcus et al., 1997[230]	EMDR (NR) Usual care (NR)	NR - Variable number of sessions (none)	Male and female Mixed	IES 46.1 to 49.7	42	79 34
Power et al., 2002[243]	EMDR (39) EXP+CR (37) Waitlist (29)	10 weeks (15 months)	Male and female Mixed	IES 32.6 to 35.1	40	42 NR
Zimmerman et al., 2007[264]	EMDR (40) Usual care (49)	Twice a week for 68 days (12 to 60 months)	Male and female Mixed (91% male, German soldiers)	IES 36.1 NR	28	9 NR

[a] The number of participants randomized to each active treatment group was not reported. A total of 27 participants from the active treatment groups were analyzed, 9 in each treatment group.

CAPS = Clinician-Administered Post Traumatic Stress Disorder Scale; CBT-M = cognitive behavioral therapy-mixed; CI = confidence interval; CR = cognitive restructuring; EFT = Emotional Freedom Techniques; EMDR = eye movement desensitization and reprocessing; F = female; IES = Impact of Event Scale; MISS = Mississippi Scale for Combat-Related Post Traumatic Stress Disorder; N = number; NR = not reported; PE = prolonged exposure; PTSD = posttraumatic stress disorder; PSS-SR = Post Traumatic Stress Disorder Symptom Scale-Self-Report; SITPE = stress inoculation training with prolonged exposure; y = year.

Analyses of Other Psychological Interventions

Ten trials that we rated high risk of bias dealt with a variety of other psychological interventions (Table G-6). Three of these assessed narrative exposure therapy (NET); of these three, the one comparing NET with usual care found results consistent with those from medium risk-of-bias trials. The other two NET trials had active comparators -- stress inoculation therapy and psychoeducation. Whereas the IPT study rated high risk of bias tested the efficacy of IPT versus treatment as usual, the IPT study included in the main study findings compared the effectiveness of IPT versus two other treatments, precluding comparisons of the findings. Other studies rated high risk of bias assessed interventions (or comparators) not included for the main analyses, namely slow breathing (SB) feedback, and trauma-focused CBT (TF-CBT) plus breathing biofeedback; thus, we could not assess, for example, the consistency of the results.

Table G-6. Characteristics of other psychological intervention trials omitted from main analyses because of high risk of bias

Trial	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female % Nonwhite
Bichescu et al., 2007[202]	NET (9) PED (9)	10 weeks— 5 NET sessions, 1 PED session (6 months)	Male and female Political detainees	CIDI - PTSD 11.4 to 11.9	69	6 NR
Brom et al.,1989[203]	TD (31) Hypno (29) PDT (29) Waitlist (23)	~4 months (given only as mean number of sessions) (3 months)	Male and female Mixed	NR	42	79 NR
Hensel-Dittman et al., 2011[216]	NET (15) SIT (13)	4 weeks (6 and 12 months)	Male and female Experienced organized violence	85.2 to 96.5	NR	NR NR
Jiang et al., 2014[220]	IPT plus TAU (27) TAU (22)	12 weeks (none), 57% had clinical PTSD	Earth quake survivors w/MDD	39.41 to 45.05	30	71 100
Krupnick et al., 2008[226]	IPT (32) Waitlist (16)	16 weeks (4 months)	Female Mixed	62.6 to 65.2	32	100 94
Niles et al., 2012[236]	MBSR (17) Psychoeducation (16)	8 weeks (6 weeks)	Combat-related	61 to 72	52	0 24
Noohi et al., 2017[237]	Neuro-feedback (15) Control (15)	25 sessions (45 days after treatment)	Males War related	IES-R 47.20 to 51.07	30 to 50	0 NR
Polak et al., 2015[247]	TF-CBT plus breathing biofeedback (4) TF-CBT (4)	5 to 18 sessions (none)	Chronic PTSD Mixed	IES-R 41.5 to 45	45	75 NR
Stenmark et al., 2013[252]	NET (51) Usual care (30)	10 sessions (1 and 6 months)	Refugees and asylum seekers from other countries living in Norway	84	35	30 100
Wagner et al., 2007[257]	BA (4) Usual care (4)	4 to 6 sessions (none)	Male and female Recently Injured	PCL 54.2 to 55.5	34	38 50
Wahbeh et al., 2016[258]	SB+biofeedback (25) Sitting quietly (25)	6 weeks (1 month)	War veterans Mixed	PCL 54 to 55	53	6 14

BA = behavioral activation; CIDI = Composite International Diagnostic Interview – PTSD section; hypno = hypnotherapy; IPT = interpersonal therapy; MBSR = mindfulness-based stress reduction; N = numbers; NET = narrative exposure therapy; NR = not reported; PCL = PTSD Checklist; PDT = psychodynamic therapy; PED = psychoeducation; PTSD = posttraumatic stress disorder; SB = slow breathing ; SIT = stress inoculation training; TD = trauma desensitization; TF-CBT = trauma-focused CBT; y = year.

Analyses of Efficacy or Comparative Effectiveness of Psychological Interventions by Patient Characteristics or Type of Trauma (Key Question 1a)

Two trials that we rated high risk of bias reported on the efficacy or comparative effectiveness of psychological interventions for individuals with versus those without certain patient characteristics (see Table G-7). These trials examined data for subgroup characteristics

(age, high dissociation and PTSD symptom severity) different from the trials we had rated medium risk of bias; this difference precluded assessment of the consistency of the results.

Table G-7. Characteristics of studies that evaluated efficacy or comparative effectiveness of interventions by patient characteristics or type of trauma omitted from main analyses because of high risk of bias

Trial	Arm (N)	Treatment Duration (Followup Post Treatment)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female % Nonwhite
Butollo et al., 2015[204]	G1: DET (74) G2: CPT (74) (only 67 analyzed)	24 sessions (6 months)	Type I Trauma Mixed Subgroup analysis: age in years at median split	IES-R 66 to 67	36	66 NR
Dorrepaal et al., 2012[207]	CBT-M ("Stabilizing group treatment") (38) Usual care (33)	20 weeks (none)	Complex PTSD and severe comorbidity Subgroup analysis: dissociation and PTSD	DTS 80 to 90	39	NR NR

CPT = cognitive processing therapy; CBT-M = cognitive behavioral therapy – mixed; DET =dialogical exposure therapy; DTS =Davidson Trauma Scale; IES-R = Impact of Event Scale - Revised; N =number; NR = not reported; PTSD = posttraumatic stress disorder; y = year

Efficacy or Comparative Effectiveness of Pharmacologic Interventions (Key Question 2)

We present descriptions of a considerable number of trials of various classes or individual drugs that we had rated high risk of bias even though they otherwise met eligibility criteria for the pharmacologic interventions (KQ 2). Tables G-8 through G-13 and G-15 are placebo-controlled trials; Table G-14 is a trial testing a head-to-head comparison of different pharmacologic agents. The specific categories of medications with high risk of bias include alpha blockers, anticonvulsants, atypical antipsychotics, benzodiazepines, SSRIs, other second generation antipsychotics, and tricyclic antidepressants (no SNRI trial was rated as high risk of bias).

Generally, the tables for these KQ 2 trials follow the formats for those above describing the psychological interventions. Data reported about PTSD severity are mean CAPS scores or a range of mean CAPS scores for the intervention and control groups unless a different source of these data is specified.

Briefly, these trials mainly had analyzed only subjects who completed treatment (i.e., the investigators did not use an intention-to-treat analysis) or had very high attrition or differential attrition rates. The trials also tended to have small sample sizes Appendix provides additional rationale for risk of bias assessments.

We comment insofar as possible on the consistency of these data with the main study findings.

Alpha Blockers

We rated two trials as high risk of bias (Table G-8). Both compared prazosin with placebo.

Table G-8. Characteristics of placebo-controlled trials of alpha blockers omitted from main analyses because of high risk of bias

Trial	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Petrakis et al., 2016[241]	G1: Prazosin (16) (50) G2: Placebo (46)	13	Veterans with alcohol dependence, Combat	71.86 to 75.86	44	6 19
Simpson et al., 2015[250]	G1: Prazosin (16 or highest tolerated dose) (15) G2: Placebo (15)	6	Adults with alcohol dependence, Mixed/multiple	PSS-I 31.5 to 31.6	43	37 60

G = group; mg = milligrams; N = number; PSS-I = Posttraumatic Stress Disorder Symptom Scale-Interview

Anticonvulsants

We rated three placebo-controlled trials as high risk of bias (Table G-9). the interventions included one trial each of divalproex, lamotrigine, and topiramate.

Table G-9. Characteristics of placebo-controlled trials of anticonvulsants omitted from main analyses because of high risk of bias

Trial	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Hamner et al., 2009[215]	Divalproex[a] (16) Placebo (13)	10	Male and female Mixed	77.1	52	4 7
Hertzberg et al., 1999[217]	Lamotrigine (25 to 500) (11) Placebo (4)	12	Male and female Mixed	SI-PTSD 44.3	43	36 71
Lindley et al., 2007[228]	Topiramate (50 to 200) (20) Placebo (20)	7	Male Combat veterans	61.6	53	0 37.5

[a] Dose not reported; serum trough between 50-125 mcg/ml.

mg = milligram; N = number; PTSD = posttraumatic stress disorder; SI-PTSD = Structured Interview for PTSD; y = year.

Atypical Antipsychotics

We found no trials of atypical antipsychotics versus placebo that met our eligibility criteria but could be rated as either low or medium risk of bias. Four trials, however, were eligible but rated high risk of bias (Table G-10). Two trials tested risperidone, and one each tested aripiprazole or quetiapine,

Table G-10. Characteristics of placebo-controlled trials of atypical antipsychotics omitted from main analyses because of high risk of bias

Trial	Arm Dose mg/Day (N)	Duration (weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Naylor et al., 2015[235]	G1: Aripiprazole (5 to 20) (7) G2: Placebo (7)	10	Veterans, Combat Trauma	82.29 to 90.60	34	36 50
Padala et al., 2006[238]	Risperidone (0.5 to 8) (11) Placebo (9)	12	Female Mixed	79.3 to 80.6	41	100 30
Rothbaum et al., 2008[248]	Risperidone (0.5 to 3) (9) Placebo (11)[a]	16	Male and female Mixed	56 to 60	34	80 30
Villarreal et al., 2016[256]	G1: Quetiapine (25 to 800) (42) G2: Placebo (38)	12	Veterans w/chronic PTSD, Combat	70.60 to 75.40	52	6 47

[a]This trial did not report the number of patients randomized in each group. Overall, 25 patients were randomized; the n reported is the number of participants analyzed in each group.

mg = milligram; N = number; NR = not reported; PTSD = posttraumatic stress disorder; y = year.

Benzodiazepines

A single trial in this drug class tested alprazolam against placebo (Table G-11). As noted in the main report, no benzodiazepine trial was rated as either low or medium risk of bias. Evidence is insufficient to determine the efficacy of benzodiazepines for improving outcomes for adults with PTSD.

Table G-11. Characteristics of placebo-controlled trials of benzodiazepines omitted from main analyses because of high risk of bias

Trial	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Braun et al., 1990[169]	Alprazolam (1.5 to 6) (7) Placebo (9)	12	Male and female Mixed	PTSD-Scale 30.0 to 30.9	38	NR NR

[a]When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

mg = milligram; N = number; NR = not reported; PTSD = posttraumatic stress disorder; PTSD-Scale = Posttraumatic Stress Disorder Scale; y = year.

Selective Serotonin Reuptake Inhibitors

Among the trials for SSRIs, one studied fluoxetine and one examined paroxetine (both against placebo) (Table G-12). A third was more complicated: sertraline combined with mirtazapine (a newer type of antidepressant in the class known as tetracyclic piperazinoazepine) against sertraline combined with placebo. Findings reported for these trials were generally consistent with what investigators found in low or medium risk-of bias trials.

Table G-12. Characteristics of placebo-controlled trials of selective serotonin reuptake inhibitors omitted from main analyses because of high risk of bias

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Hertzberg et al., 2000[178]	Fluoxetine (10 to 60) (6) Placebo (6)	12	Male Combat veterans	DTS 106 to 111	46	0 58
Marshall et al., 2007[177]	Paroxetine (10 to 60) (25) Placebo (27)	10	Male and female Mixed	82.8 to 84.2	40	67 75
Schneier et al., 2015[249]	G1: Mirtazapine (15 to 45 mg) plus sertraline (25 to 200mg) (18) G2: Sertraline (25 to 200mg) plus placebo (18)	24	Adults with chronic PTSD, Mixed/multiple	PCL 58.9 to 60.0	40	64 75

[a]When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

DTS = Davidson Trauma Scale; mg = milligram; N = number; PCL = PTSD = posttraumatic stress disorder; y = year.

Other Second-Generation Antidepressants

We rated one trial comparing nefazodone (a phenylpiperazine antidepressant) with placebo as high risk of bias (Table G-13).

Table G-13. Characteristics of placebo-controlled trials of other second-generation antidepressants omitted from main analyses because of high risk of bias

Trial	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
Davis et al., 2004[205]	Nefazodone (100 to 600) (27) Placebo (15)	12	Male and female Mixed	81.0 to 83.2	54	2.4 46

Abbreviations: mg = milligram; N =number; PTSD = posttraumatic stress disorder; y = year.

One trial of nefazodone and an active comparator – sertraline (an SSRI) – was rated high risk of bias (Table G-14).

Table G-14. Characteristics of one head-to-head pharmacotherapy trial omitted from main analyses because of high risk of bias

Study	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity[a]	Mean Age (Y)	% Female % Nonwhite
McRae et al., 2004[233]	Nefazodone (100 mg to 600 mg) (18) Sertraline (50 mg to 200 mg) (19)	12	Male and female Outpatient special mental health	68.9 to 73.8	40	77 NR

[a]When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

mg = milligram; N = number; NR = not reported; PTSD = posttraumatic stress disorder; Y= year.

Tricyclic Antidepressants

We rated three trials of otherwise meeting criteria for this section as high risk of bias (Table G-15). All were placebo-controlled trials conducted more than 20 years ago: one of amitriptyline, one of imipramine, and one of desipramine.

Table G-15. Characteristics of placebo-controlled trials of tricyclic antidepressants omitted from main analyses because of high risk of bias

Trial	Arm Dose mg/Day (N)	Duration (Weeks)	Population Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female %Nonwhite
Davidson et al., 1990[179] Davidson et al., 1993[180]	Amitriptyline (50 to 300) (33) Placebo (29)	8	NR Combat veterans	IES 33.1	49	NR NR
Kosten et al., 1991[182]	Imipramine (50 to 300) (23) Placebo (19)	8	Male Combat veterans	IES 35.6	39	0 NR
Reist et al., 1989[181]	Total (27) Desipramine (50 to 200) (NR) Placebo (NR)	4	Male Combat veterans	IES 55.2 to 56.2	38	0 NR

Note: When mean data for baseline PTSD severity were not reported for the total sample but were presented for each study arm, we provide the range across arms.

F = female; IES = Impact of Event Scale; mg = milligram; N = total number randomized/assigned to intervention and control groups; NR = not reported; PTSD = posttraumatic stress disorder; y = year.

Psychotherapy Versus Pharmacotherapy for Adults With Posttraumatic Stress Disorder (Key Question 3)

Of the two trials bias that attempted to address KQ 3and that we rated as high risk of bias (Table G-16) one trial compared paroxetine with CBT and the other trial compared paroxetine with PE therapy. As with the information for KQ 1 and KQ 2, disease severity is measured by CAPS unless another source is specified. Prolonged exposure plus paroxetine was not a combined intervention of interest for KQ 3 because it tested a combined psychotherapy and pharmacology intervention.

Table G-16. Characteristics of studies directly comparing pharmacotherapies and psychotherapies omitted from main analyses because of high risk of bias

Study	Arm (N)	Treatment Duration (Followup)	Population, Trauma Type	Baseline PTSD Severity	Mean Age (Y)	% Female %Nonwhite
Frommberger et al., 2004[212]	Paroxetine (11)[a] CBT (10)	12 weeks (3 and 6 months)	Male and female, Mixed	70.5	43	57 NR
Popiel et al., 2015[242]	Paroxetine (57)[b] PE (114) Paroxetine + PE (57) (group not of interest to this KQ)	12 weeks (1 yr)	Male and female, Motor vehicle accident	SCID-I symptoms: 11.7 to 11.8	39	22 NR

[a] Titrated from 10 mg/day to max 50 mg/day (mean = 28 mg/day).
[b] A dose of 20 mg/day was achieved in 3 to 7 days.

CBT = cognitive behavioral therapy; mg = milligram; N = number; NR = not reported; PE = prolonged exposure; PTSD = posttraumatic stress disorder; SCID-I = Structured Clinical Interview for Axis I Disorders; yr = year.

Both trials found that participants in the psychological intervention groups (CBT and PE) experienced greater reductions in PTSD symptoms than those in the paroxetine groups. These findings are consistent with those from a medium risk-of-bias trial in our analyses, which compared EMDR with fluoxetine.

Appendix H. Meta-Analysis Forest Plots

Key Question 1

CBT-Mixed: Meta-Analysis Results

Figure H-1. Standardized mean change from baseline in PTSD symptoms (CAPS, PSS-I, IES, PCL, PDS) for CBT-mixed compared with inactive comparators

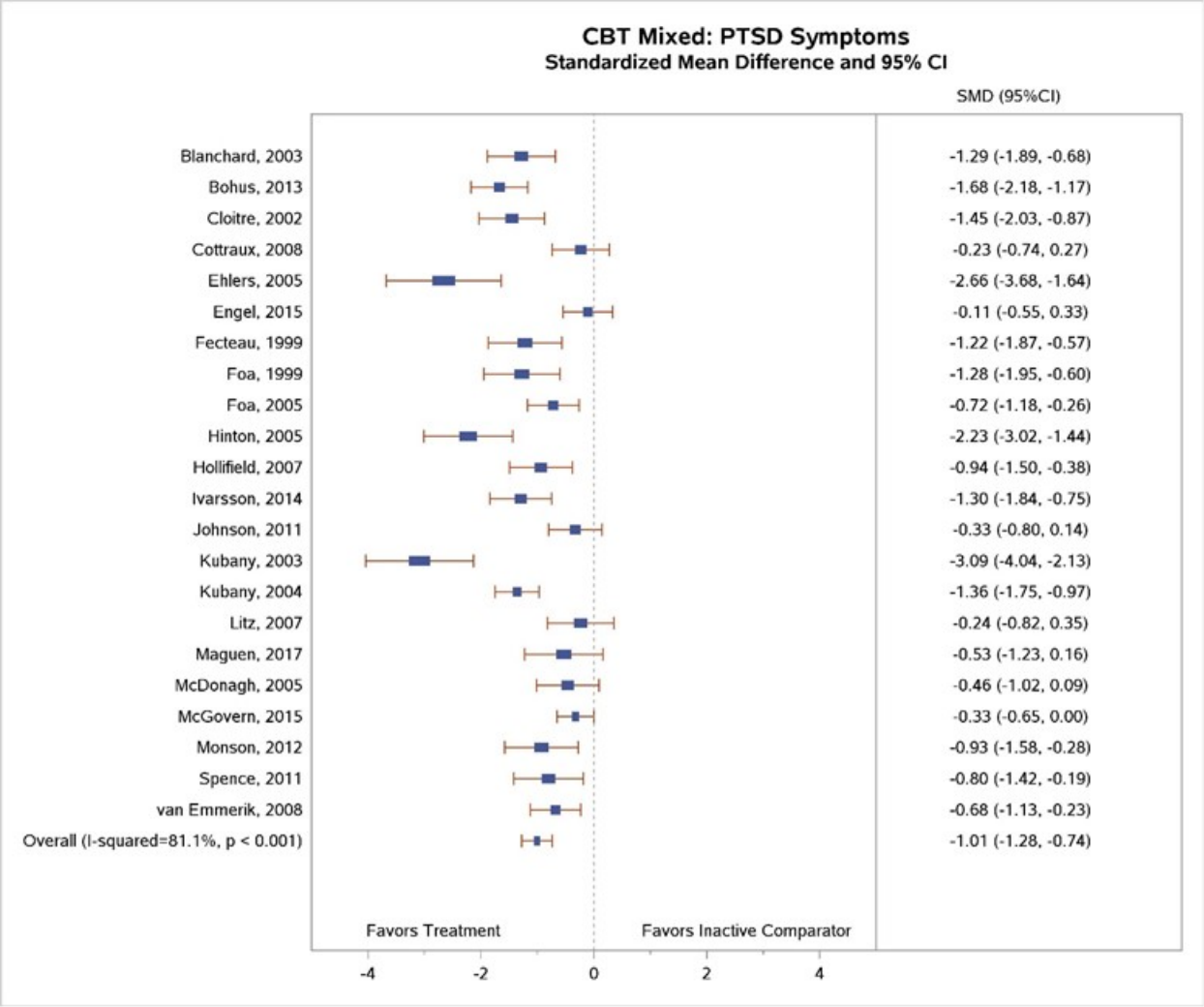


Figure H-2. Standardized mean change from baseline in CAPS for CBT-mixed compared with inactive comparators at 3 to 6-month followup

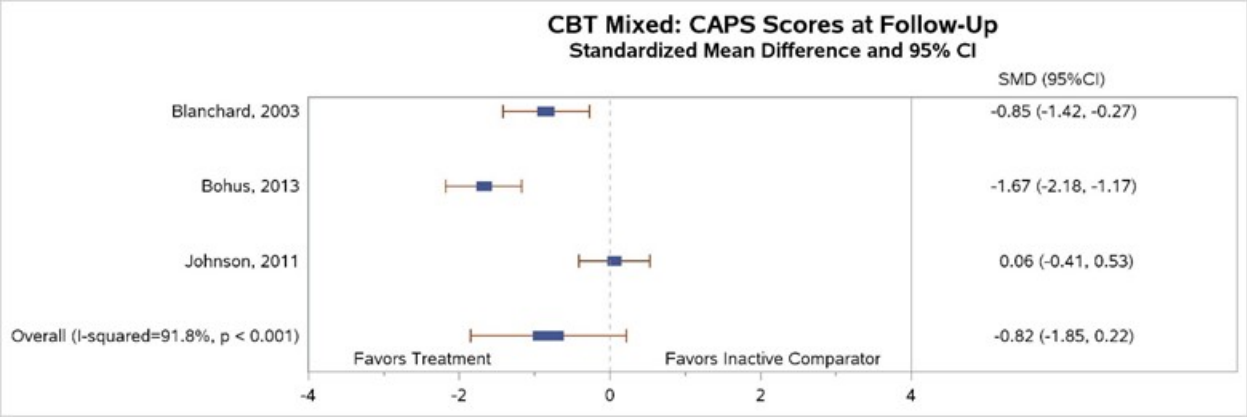


Figure H-3. Standardized mean change from baseline in PTSD symptoms for CBT-mixed compared with inactive comparators at 3 to 6-month followup

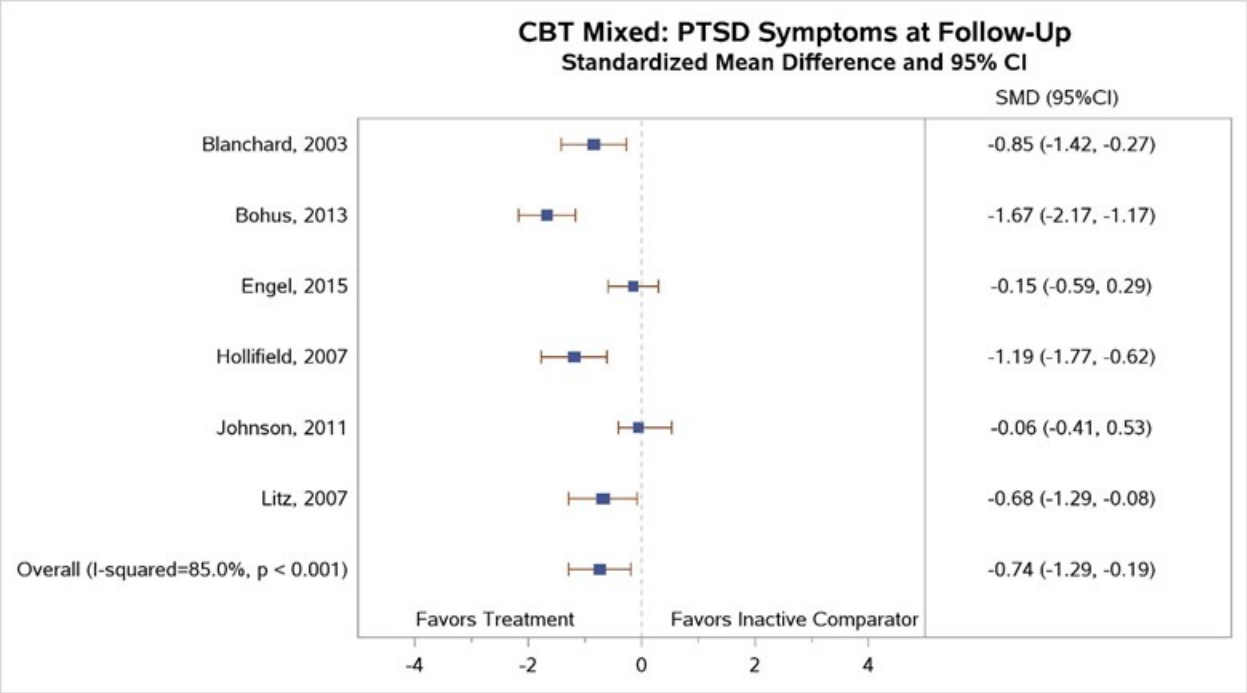


Figure H-4. Standardized mean change from baseline in depressive symptoms (measured by BDI) for CBT-mixed compared with inactive comparators

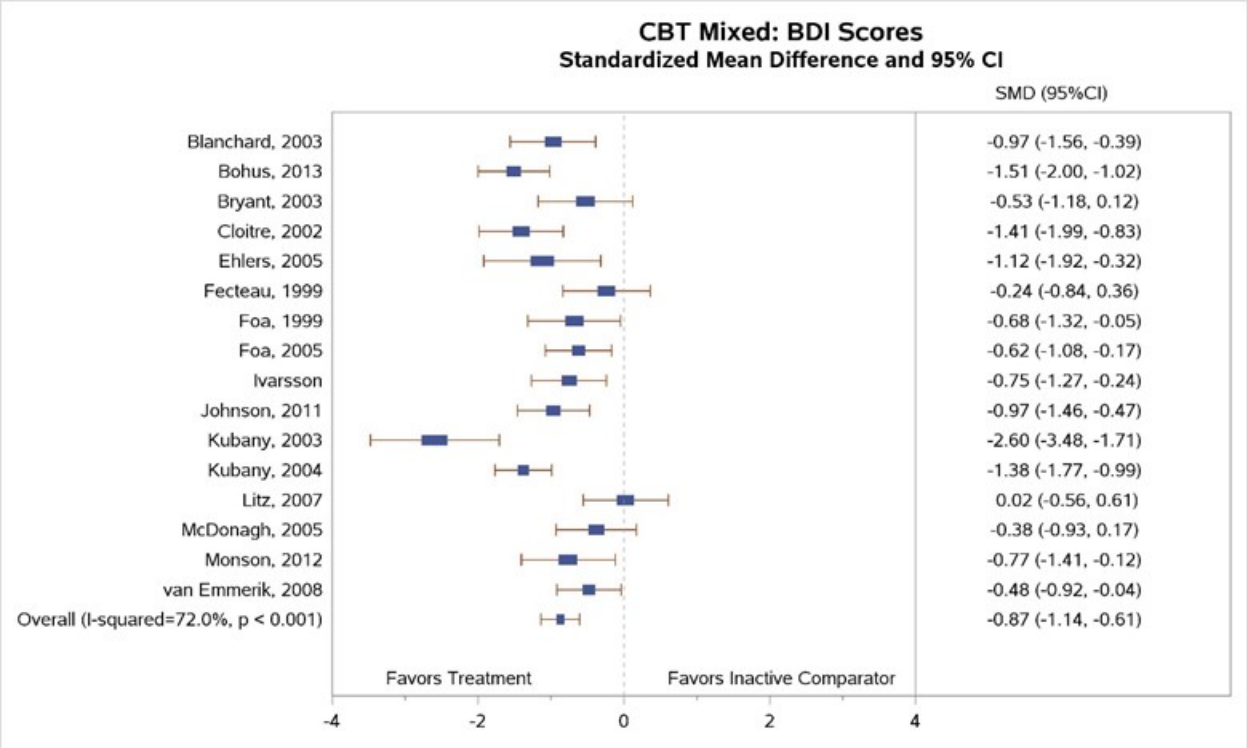


Figure H-5. Standardized mean change from baseline in depressive symptoms (measured by BDI) for CBT-mixed compared with inactive comparators at 3 to 6-months

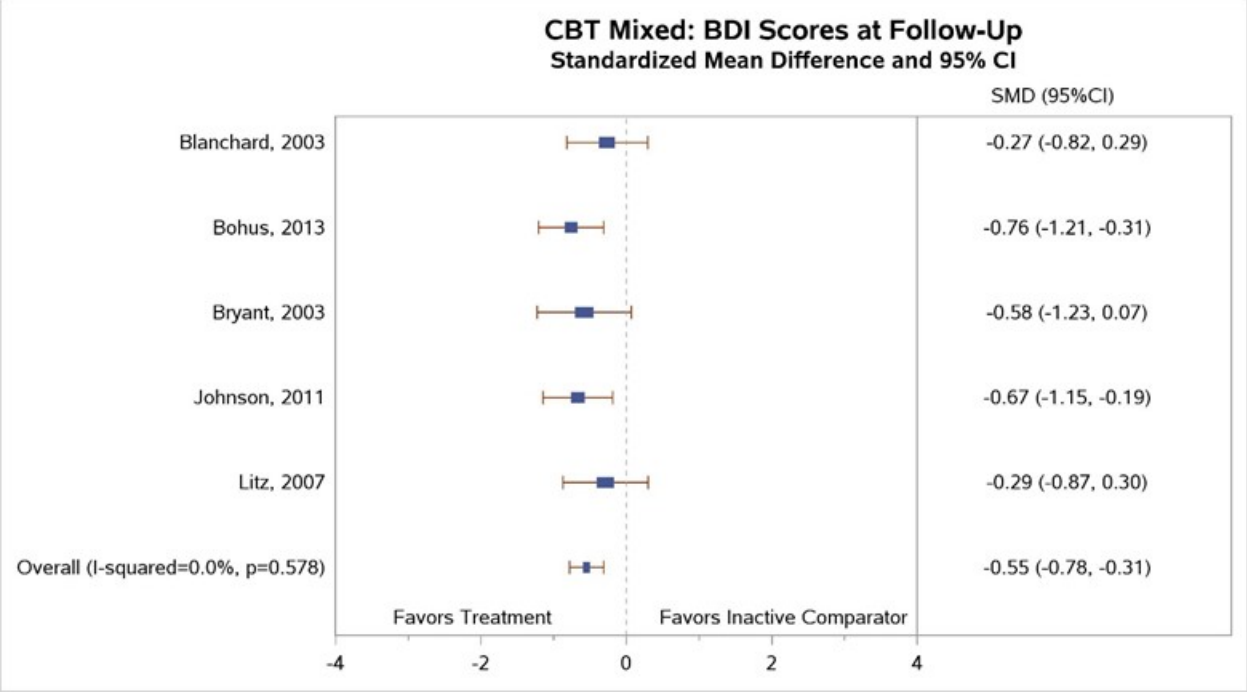
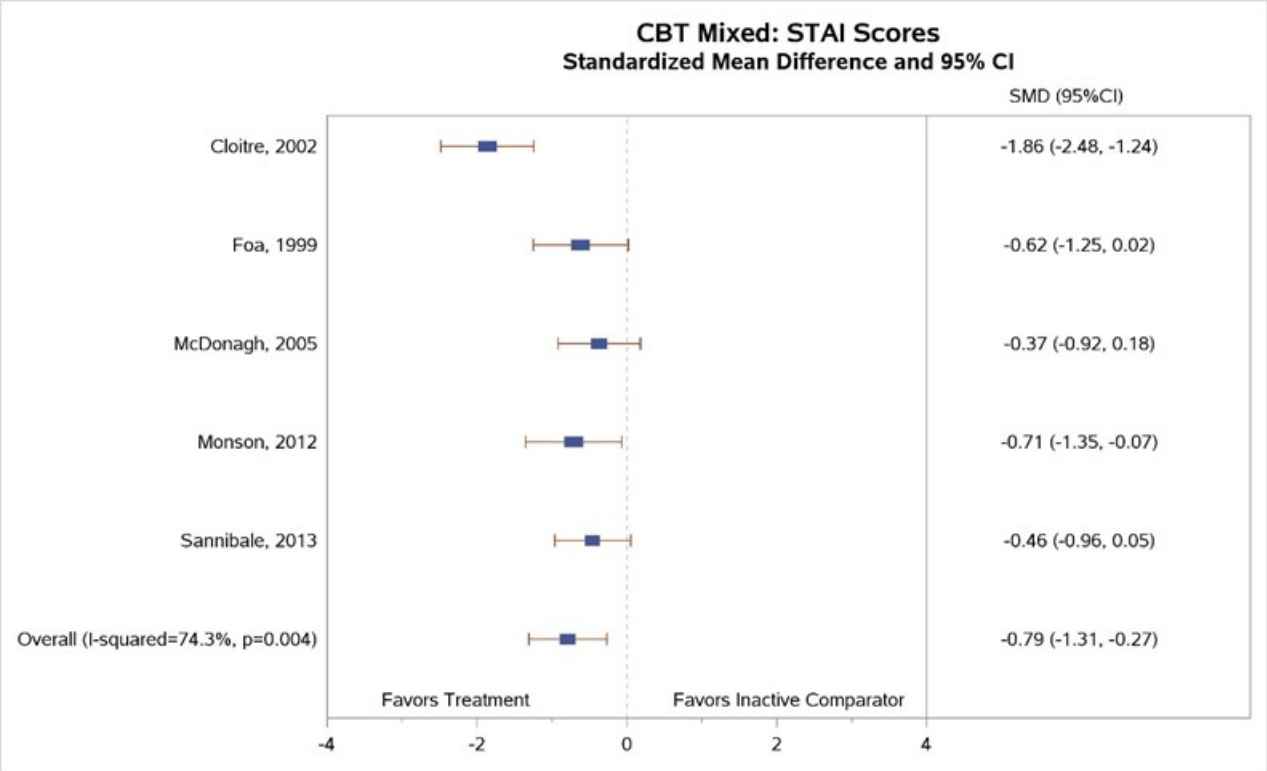


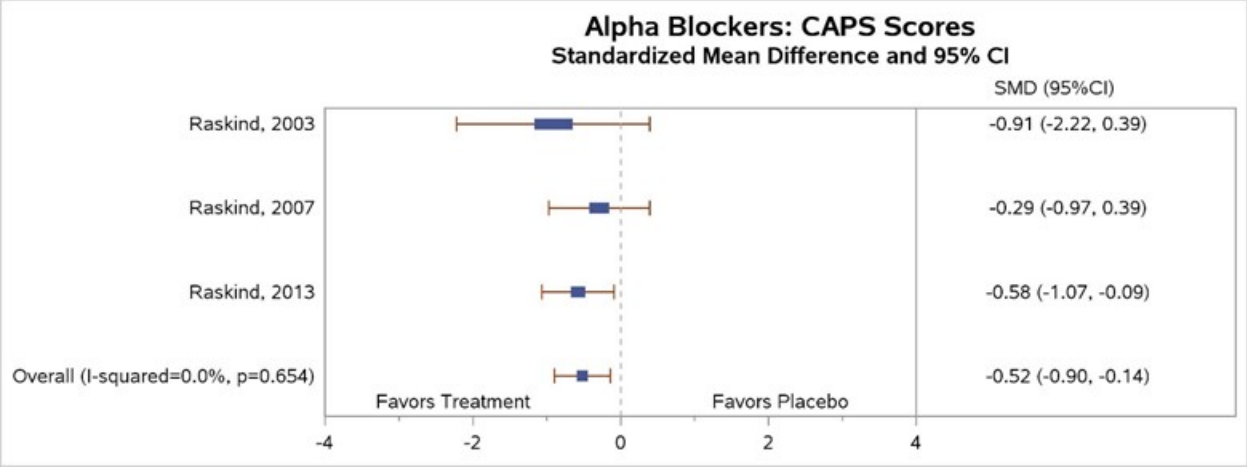
Figure H-6. Standardized mean change from baseline in anxiety symptoms (measured by STAI) for CBT-mixed compared with inactive comparators



Key Question 2

Alpha-Blockers: Meta-Analysis Results

Figure H-7. Standardized mean change from baseline in CAPS for prazosin compared with placebo



SNRIs: Meta-Analysis Results

Figure H-8. Standardized mean difference from baseline in CAPS for venlafaxine compared with placebo

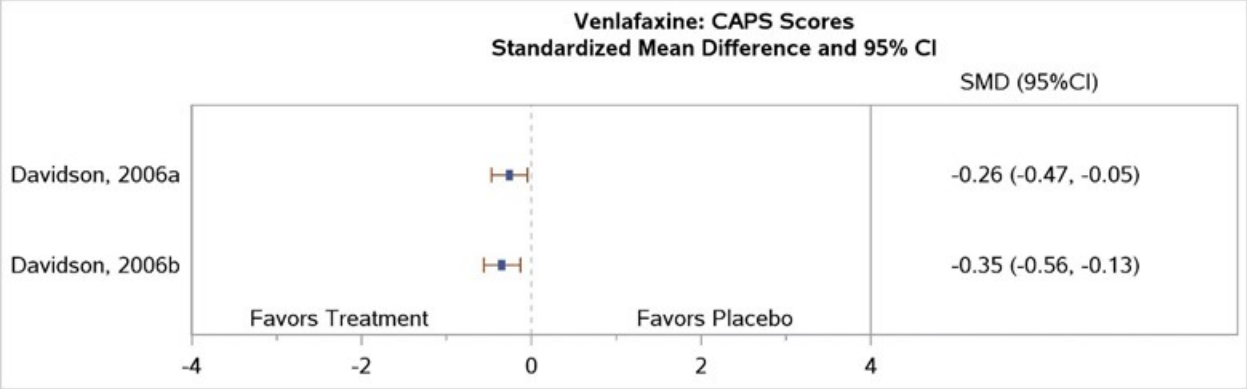
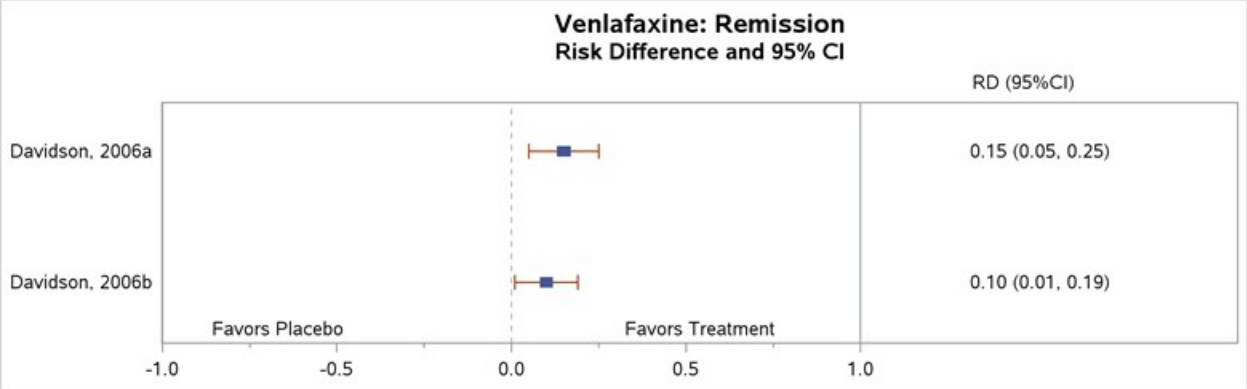


Figure H-9. PTSD remission for venlafaxine compared with placebo



Key Question 4

Withdrawals Due to Adverse Events: Meta-Analysis Results

Figure H-10. Withdrawals due to adverse events for anticonvulsants compared with placebo

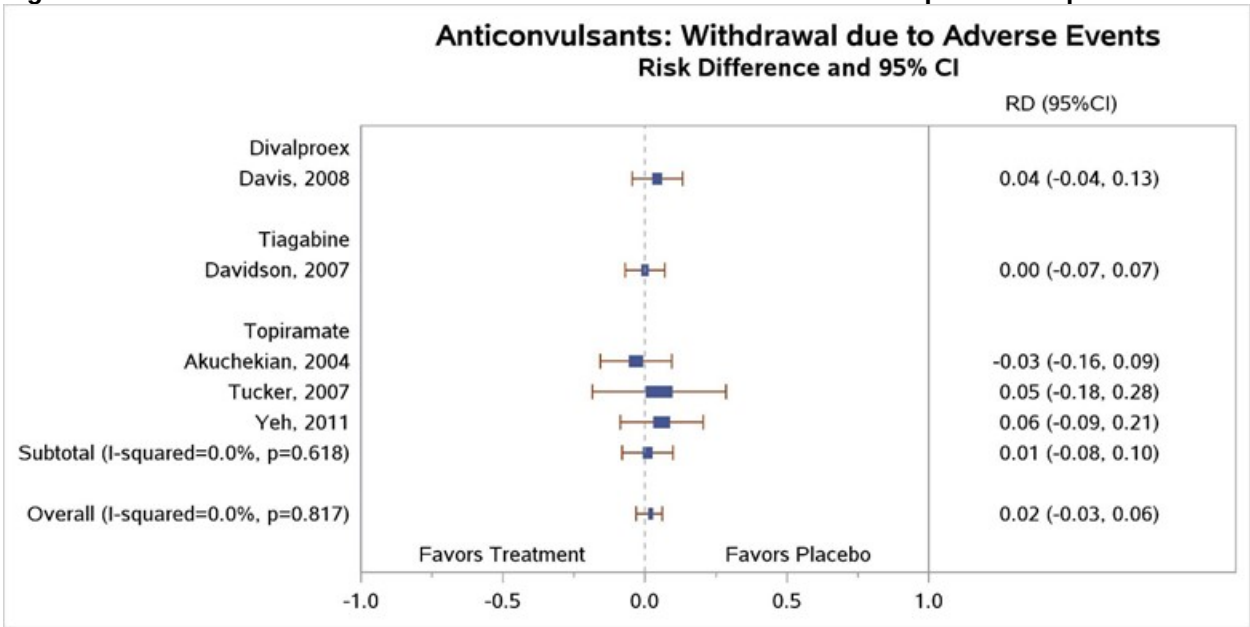


Figure H-11. Withdrawals due to adverse events for antipsychotics compared with placebo

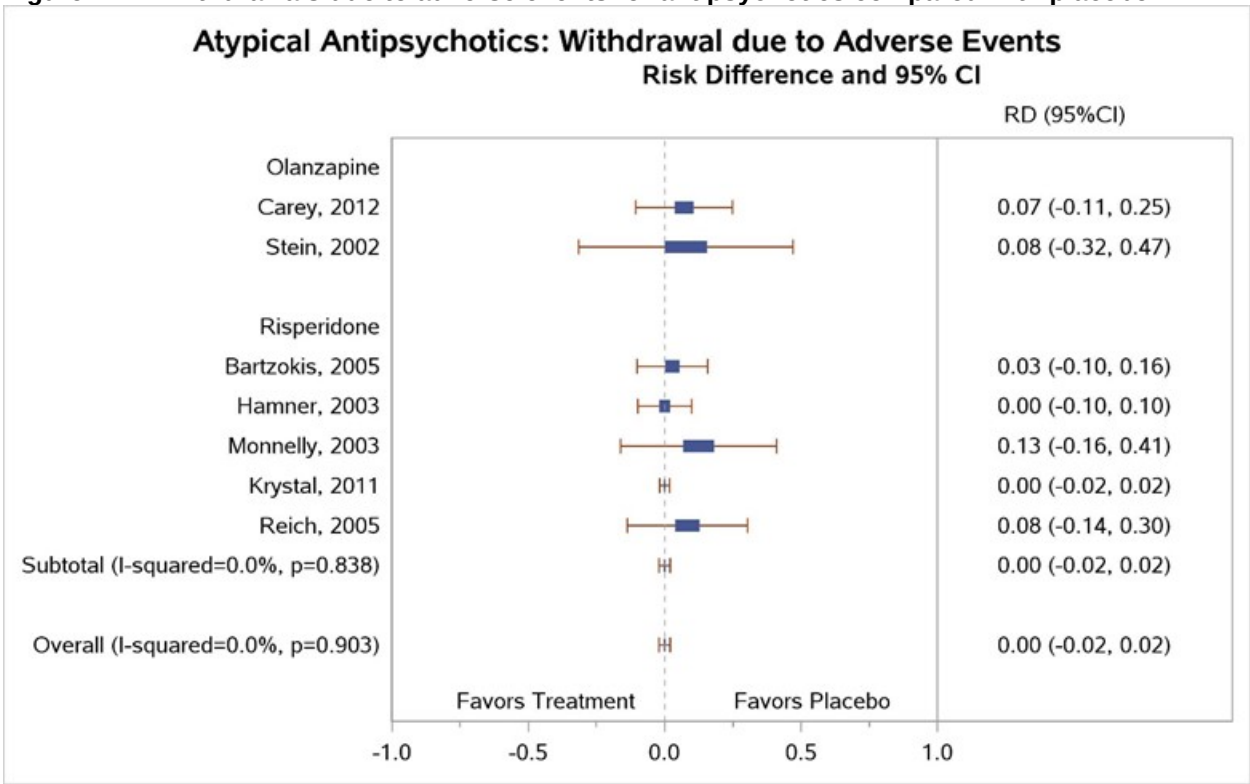
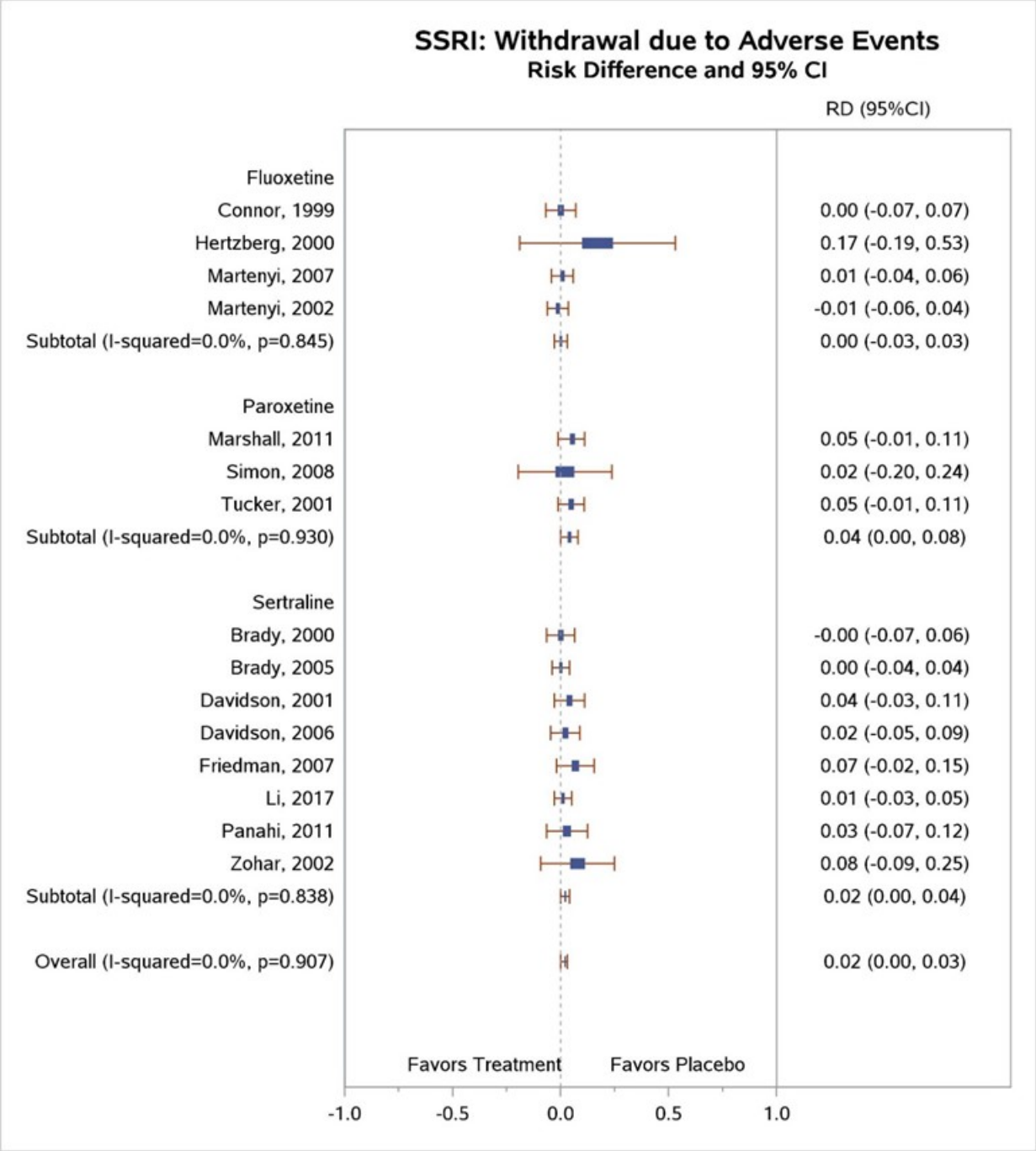
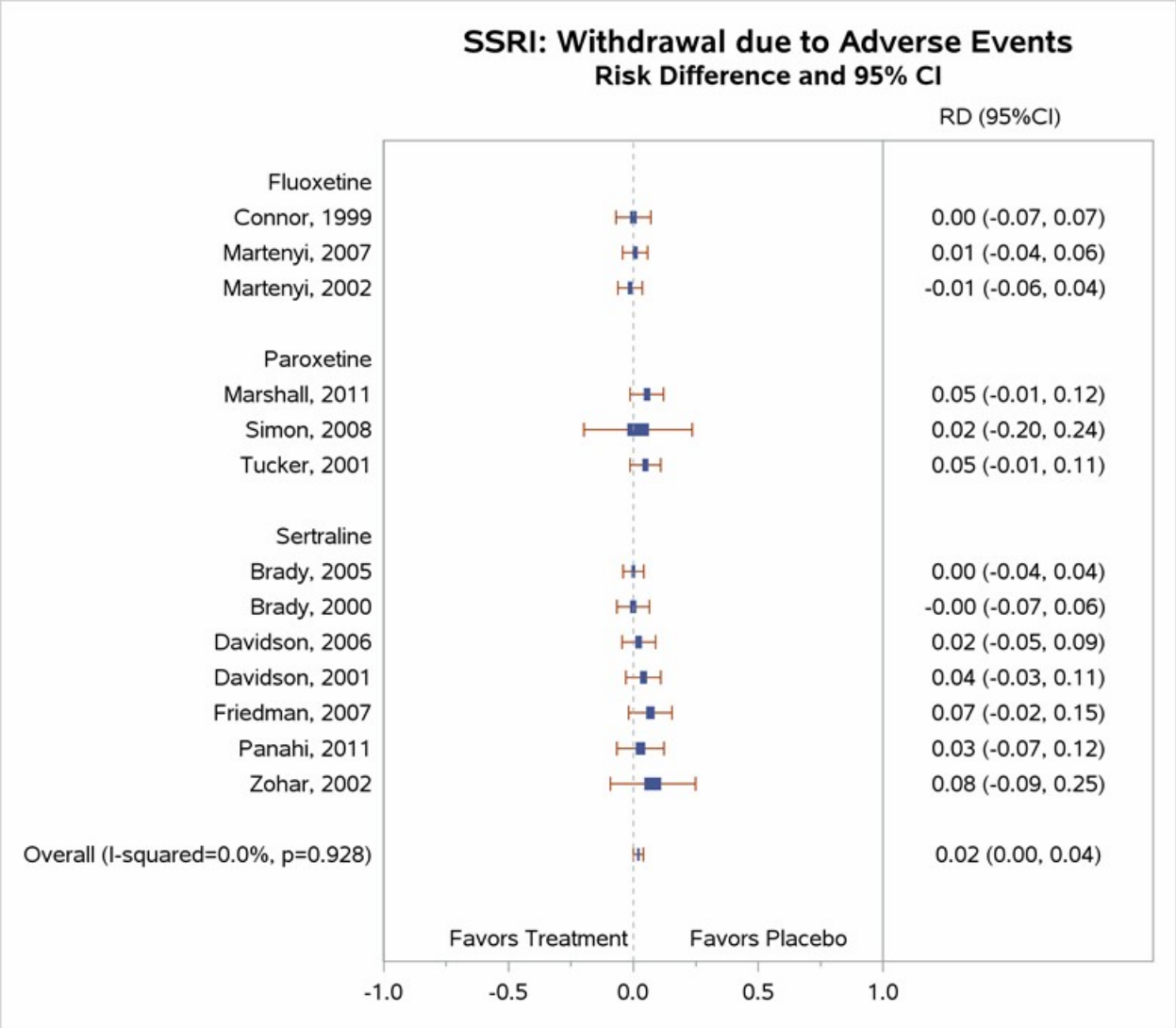


Figure H-12. Withdrawals due to adverse events for SSRIs compared with placebo




SSRI: Withdrawal due to Adverse Events
Risk Difference and 95% CI
RD (95%CI)
Fluoxetine
Connor, 1999
0.00 (-0.07, 0.07)
Martenyi, 2007
0.01 (-0.04, 0.06)
Martenyi, 2002
-0.01 (-0.06, 0.04)
Paroxetine
Marshall, 2011
0.05 (-0.01, 0.12)
Simon, 2008
0.02 (-0.20, 0.24)
Tucker, 2001
0.05 (-0.01, 0.11)
Sertraline
Brady, 2005
0.00 (-0.04, 0.04)
Brady, 2000
-0.00 (-0.07, 0.06)
Davidson, 2006
0.02 (-0.05, 0.09)
Davidson, 2001
0.04 (-0.03, 0.11)
Friedman, 2007
0.07 (-0.02, 0.15)
Panahi, 2011
0.03 (-0.07, 0.12)
Zohar, 2002
0.08 (-0.09, 0.25)
Overall (I-squared=0.0%, p=0.928)
0.02 (0.00, 0.04)
Favors Treatment
Favors Placebo
-1.0
-0.5
0.0
0.5
1.0

Appendix I. Strength of Evidence

Key Question 1

Table I-1. Cognitive processing therapy compared with inactive controls (waitlist or usual care)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline to end of treatment in CAPS						
5; 399	Medium; RCTs	Consistent	Direct	Imprecise	SMD -1.35 (95% CI, -1.77 to -0.94)	Moderate
Loss of Diagnosis						
4; 299	Medium; RCTs	Consistent	Direct	Imprecise	RD 0.44 (95% CI, 0.26 to 0.62)	Moderate
Prevention/reduction of comorbid depression: mean change from baseline to end of treatment in BDI						
5; 399	Medium; RCTs	Consistent	Direct	Precise	SMD -1.09 (95% CI, -1.52 to -0.65)	Moderate
Prevention/reduction of comorbid anxiety: mean change from baseline to end of treatment in STAI						
2; 119	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial significantly favored CPT, the other found no differences	Insufficient
Quality of Life						
2; 159	Medium; RCT	Inconsistent	Direct	Imprecise	One trial significantly favored CPT, the other found no differences in physical quality of life measures	Insufficient

CAPS = Clinician Assessment PTSD Scale; CI = confidence interval; CPT = cognitive processing therapy; CR = cognitive restructuring; NA = not applicable; NNT = number needed to treat; RA = repeated assessments (a type of waitlist control group); RCT = randomized controlled trial; RD = risk difference; STAI = State-Trait Anxiety Inventory; UC = usual care; WL = waitlist

Table I-2. Cognitive therapy compared with inactive controls (waitlist or usual care)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline to end of treatment						
4; 236	Medium; RCTs	Consistent	Direct	Imprecise	SMD range -2.0 to -0.3, p<0.05 for 4 of 4 trials.	Moderate
Loss of Diagnosis						
4; 283	Medium; RCTs	Consistent	Direct	Imprecise	RD 0.55 (95% CI, 0.28 to 0.82)	Moderate
Prevention/reduction of comorbid depression: mean change from baseline to end of treatment on BDI						
4; 283	Medium; RCTs	Consistent	Direct	Imprecise	WMD range -11.1 to -8.3 N=283, p<0.05 for 4 of 4 trials.	Moderate
Prevention/reduction of comorbid anxiety: mean change from baseline to end of treatment in BAI						
4; 284	Medium; RCTs	Consistent	Direct	Imprecise	WMD range -5.6 to -18.7, p<0.05 for 3 of 4 trials	Moderate
Quality of Life						
2; 199	Medium; RCT	Inconsistent	Direct	Imprecise	One trial significantly favored CT, the other found no differences in mental quality of life measures	Insufficient
Disability/functional impairment; mean change in SDS from baseline to posttreatment						
3; 176	Medium; RCTs	Consistent	Direct	Precise	WMD range -11.3 to -2.2, p<0.05 for 3 of 3 trials	Moderate

[a]Included trials compared CT with waitlist (Ehlers 2003 and Ehlers 2005), a self-help booklet (Ehlers 2003), and usual care (Muesser 2008).

[b]Data were based on meta-analysis of CAPS total for Muesser 2008 and CAPS-intensity for the Ehlers 2003 and 2005 studies.

[c]Direction of effects were consistent; magnitude of effects ranged from very large to small

BAI = Beck Anxiety Inventory; CI = confidence interval; NA = not applicable; NNT = number needed to treat; RCT = randomized controlled trial; RD = risk difference; WL = waitlist.

Table I-3. Metacognitive therapy compared with inactive controls (waitlist or usual care)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline to end of treatment						
1; 21	Medium; RCTs	NA, single study	Direct	Imprecise	WMD -27.7	Insufficient
Prevention/reduction of comorbid depression: mean change from baseline to end of treatment in BDI						
1; 21	Medium; RCTs	NA, single study	Direct	Imprecise	Findings favor MCT, p<0.05	Insufficient
Prevention/reduction of comorbid anxiety: mean change from baseline to end of treatment in BAI						
1; 21	Medium; RCTs	NA, single study	Direct	Imprecise	Findings favor MCT, p<0.05	Insufficient

BAI = Beck Anxiety Inventory; CI = confidence interval; NA = not applicable; NNT = number needed to treat; RCT = randomized controlled trial; RD = risk difference; WL = waitlist.

Table I-4. Stress inoculation training compared with waitlist

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: PSS-I						
1; 41	Medium; RCT	NA, single study	Direct	Imprecise	WMD -10.5, p<0.05	Insufficient
Loss of Diagnosis						
1; 41	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.42, p<0.05	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 41	Medium; RCT	NA, single study	Direct	Imprecise	WMD -8.5, p<0.05	Insufficient
Prevention/reduction of comorbid anxiety: STAI						
1; 41	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -11.4, p=ns	Insufficient

BDI = ; CI = confidence interval; NA = not applicable; PSS-I = Posttraumatic Stress Disorder Symptom Scale-Interview; RCT = randomized controlled trial

Table I-5. Relaxation compared with treatment as usual

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction						
1; 25	Medium; RCT	NA, single study	Direct	Imprecise	p=ns for 3 different measures	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 25	Medium; RCT	NA, single study	Direct	Imprecise	Favor relaxation but significance not reported	Insufficient
Prevention/reduction of comorbid anxiety: STAI						
1; 25	Medium; RCT	NA, single study	Direct	Imprecise	Favor relaxation but p=ns	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-6. Relaxation compared with cognitive restructuring

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: percentage of patients with at least 50% decrease in PSS symptoms at posttreatment						
1; 34[a]	Medium; RCT	NA, single study	Direct	Imprecise	RD, 0.17 favoring CR, p=*ns*	Insufficient
Loss of Diagnosis						
1; 34[a]	Medium; RCT	NA, single study	Direct	Imprecise	RD, 0.10 favoring CR, p=*ns*	Insufficient
Prevention/reduction of comorbid depression: BDI, mean change scores (improvement)						
1; 34[a]	Medium; RCT	NA, single study	Direct	Imprecise	WMD -5.0 favoring CR, p=ns	Insufficient
Prevention/reduction of comorbid anxiety						

[a] Total trial N was 81. Subjects were randomized to PE (23), CR (13), CBT- Mb (CR+PE) (24), or relaxation (21).[122]

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-7. Mindfulness Based Stress Reduction compared with treatment as usual

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: PCL						
1; 50	Medium; RCT	NA, single study	Direct	Imprecise	WMD -3.0, p<0.05	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 50	Medium; RCT	NA, single study	Direct	Imprecise	WMD –2.8, p<0.05	Insufficient

CI = confidence interval; NA = not applicable; PSS-I = Posttraumatic Stress Disorder Symptom Scale-Interview; RCT = randomized controlled trial

Table I-8. Neurofeedback training compared with waitlist

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 52	Medium; RCT	NA, single study	Direct	Imprecise	WMD -20.3, p<0.05; also significant decreases in DTS scores	Insufficient
Loss of Diagnosis						
1; 52	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.40, p<0.05	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 41	Medium; RCT	NA, single study	Direct	Imprecise	WMD -8.5, p<0.05	Insufficient
Prevention/reduction of comorbid anxiety: STAI						
1; 41	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -11.4, p=ns	Insufficient

CI = confidence interval; NA = not applicable; PSS-I = Posttraumatic Stress Disorder Symptom Scale-Interview; RCT = randomized controlled trial

Table I-9. Exposure-based therapies compared with inactive controls (waitlist or usual care)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS and all PTSD symptom measures						
13; 885 (all); 8; 689 (CAPS)	Medium; RCTs	Consistent	Direct	Precise	SMD -1.23 (95% CI, -1.50 to -0.97) SMD (CAPS) -1.12 (95% CI, -1.42 to -0.82	High
Loss of Diagnosis						
6; 409	Medium; RCTs	Consistent	Direct	Precise	RD 0.56 (95% CI, 0.35 to 0.78)	High
Prevention/reduction of comorbid depression: BDI						
10 ; 715	Medium; RCTs	Consistent	Direct	Precise	SMD -0.76 (95% CI, -0.91 to -0.60)	High
Prevention/reduction of comorbid anxiety						
3; 286	N/A	Consistent	Direct	Imprecise	All favored CBT-exposure, p<0.05 for 2 of 3	Low
Disability/functional impairment						
2; 221[a]	Medium; RCTs	Inconsistent	Direct	Imprecise	Small trial (N=31) favored CBT-exposure, p<0.05 but other larger trial found no differences, p=ns	Insufficient

[a] One trial did not provide sample sizes of each group, so this total includes the PE+CR group which was not included in this analysis.

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-10. Exposure-based therapy compared with cognitive restructuring

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 38	Medium; RCT	NA, single study	Direct	Imprecise	p<0.05	Insufficient
Loss of Diagnosis						
1; 38	Medium; RCT	NA, single study	Direct	Imprecise	p<0.05	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 38	Medium; RCT	NA, single study	Direct	Imprecise	p<0.05	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-11. Exposure-based therapy compared with cognitive therapy

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1;62	Medium; RCT	NA, single study	Direct	Imprecise	WMD -4.0, p<0.05	Insufficient
Loss of Diagnosis						
1; 62	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.16, p<0.05	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 62	Medium; RCT	NA, single study	Direct	Imprecise	WMD -1.9, p<0.05	Insufficient
Prevention/reduction of comorbid anxiety						
1; 62	Medium; RCT	NA, single study	Direct	Imprecise	P<0.05	Insufficient
Return to work or return to active duty: % of subjects actively working at 6 month follow up						
1; 62	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.07, p=ns	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-12. Exposure-based therapy compared with cognitive processing therapy

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 124	Medium; RCT	NA, single study	Direct	Imprecise	WMD -4.0, p=ns	Insufficient
Loss of Diagnosis						
1; 124	Medium; RCT	NA, single study	Direct	Imprecise	WMD 0, p=ns	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 124	Medium; RCT	NA, single study	Direct	Imprecise	WMD -2.9, p=ns	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-13. Exposure-based therapy compared with metacognitive therapy

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: PDS						
1; 22	Medium; RCT	NA, single study	Direct	Imprecise	WMD -10.5, p<0.05	Insufficient
Loss of Diagnosis						
1;22	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.30, unknown statistical significance	Insufficient
Prevention/reduction of comorbid depression: BDI						
1;22	Medium; RCT	NA, single study	Direct	Imprecise	WMD -7.6, p<0.05	Insufficient
Prevention/reduction of comorbid anxiety: BAI						
1;22	Medium; RCT	NA, single study	Direct	Imprecise	WMD -4.7, p<0.05	Insufficient

BAI = Beck Anxiety Inventory; BDI = Beck Depression Inventory; CI = confidence interval; NA = not applicable; RCT = randomized controlled trial.

Table I-14. Exposure-based therapy compared with stress inoculation training

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 51	Medium; RCT	NA, single study	Direct	Imprecise	WMD -1.8, p=ns	Insufficient
Loss of Diagnosis						
1; 51	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.18, p=ns	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 51	Medium; RCT	NA, single study	Direct	Imprecise	WMD -0.2, p=ns	Insufficient

NA = not applicable

Table I-15. Exposure-based therapy compared with relaxation

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
3; 155	Medium; RCTs	Consistent	Direct	Imprecise	SMD -0.45 (-0.78 to -0.13)3, 3 trials, N=155	Moderate
Loss of Diagnosis						
2; 85	Medium; RCTs	Consistent	Direct	Imprecise	RD range 0,20 to 0.47, both trials favored CBT-exposure, p<0.05 in 2 of 2 trials	Moderate
Prevention/reduction of comorbid depression: BDI or HAM-D						
3; 155	Medium; RCTs	Consistent	Direct	Imprecise	SMD -0.39 (-0.71 to -0.07), 3 trials, N=155	Moderate

NA = not applicable

Table I-16. Exposure-based therapy compared with EMDR

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
3; 199	2 Medium, 1 Low; RCTs	Consistent	Direct	Imprecise	P=ns in 3 of 3 trials	Low for no difference
Symptom Remission						
0; 0	NA	NA	NA	NA	NA	Insufficient
Loss of Diagnosis						
3; 199	2 Medium, 1 Low; RCTs	Inconsistent	Direct	Imprecise	No significant difference between groups, 2 of 3 favored PE and 1 of 3 favored EMDR	Insufficient
Prevention/reduction of comorbid depression: BDI						
2; 91	Medium; RCTs	Consistent	Direct	Imprecise	P=ns	Insufficient

CI = confidence interval; NA = not applicable; PE = prolonged exposure; RCT = randomized controlled trial

Table I-17. Exposure-based therapy compared with IPT

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 78	Medium; RCT	NA, single study	Direct	Imprecise	p=ns	Insufficient
Symptom Remission						
1;78	NA	NA, single study	NA	NA	RD 0.03, p=ns	Insufficient
Prevention/reduction of comorbid depression: HAM-D						
1;78	Medium; RCT	NA, single study	Direct	Imprecise	p=ns	Insufficient
Quality of Life						
1; 78	Medium, RCT	NA, single study	Direct	Imprecise	No significant difference between PE and IPT (-17.9 vs. -11.3, p=0.061)	Insufficient

CI = confidence interval; NA = not applicable; PE = prolonged exposure; RCT = randomized controlled trial

Table I-18. Exposure-based therapy compared with exposure therapy + cognitive restructuring

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS or PSS-I						
4; 299	Medium; RCTs	Inconsistent	Direct	Imprecise	Two studies favored exposure + CR, one study favored CR; p=ns for 4 of 4 trials	Insufficient
Loss of Diagnosis						
3; 146	Medium; RCTs	Imprecise	Direct	Imprecise	P=ns for 3 of 3 studies, one favored PE and two favored PE+CR	Insufficient
Prevention/reduction of comorbid depression: BDI						
4; 299	Medium; RCTs	Consistent	Direct	Imprecise	P=ns in 4 of 4 studies	Low for no benefit

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-19. CBT-mixed interventions compared with inactive controls (waitlist, usual care)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency[a]**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline to end of treatment for CAPS, all PTSD symptom measures						
11; 709 (CAPS) 21; 1349 (all PTSD symptom measures)	Medium; RCTs	Consistent	Direct	Precise	SMD -1.01 (95% CI, -1.28 to -0.74) SMD (CAPS) -1.24 (95% CI, -1.67 to -0.81)	High
Remission (PCL)						
1; 44	Medium; RCTs	NA, single study	Direct	Imprecise	0.40	Insufficient
Loss of Diagnosis						
9; 474	Medium; RCTs	Consistent	Direct	Precise	RD 0.29 (0.17, 0.40)	High
Prevention/reduction of comorbid depression: mean change from baseline in BDI						
15; 929	Medium; RCTs	Consistent	Direct	Precise	SMD -0.87 (95% CI, -1.14 to -0.61)	High
Prevention/reduction of comorbid anxiety: mean change from baseline in STAI						
5; 257	Medium; RCTs	Consistent	Direct	Imprecise	WMD, -10.4 (-18.0 to -2.8); 5 trials, N=257; I squared=82.9	Moderate
Quality of Life						
5; 416	Medium; RCTs	Inconsistent	Direct	Imprecise	Mixed results (3 of 5 no difference p=ns; 2 of 5 favored CBT-M p<0.05)	Insufficient[a]
Disability/functional impairment						
6; 350	Medium; RCTs	Consistent	Direct	Imprecise	All trials favored CBT-M, 4 of 6 met statistical significance.	Low[b]

[a] The use of four difference quality of life measures[149] across the five trials, (one of which included only subscale data, precluded the use of meta-analysis to pool findings). We downgraded the SOE grade for these inconsistencies further due to heterogeneity in measures.
[b] We did not use meta-analysis to pool findings because of the diversity of measures used to different aspects of disability and functional impairment. We downgraded the SOE grades for these inconsistencies further due to heterogeneity in measures.
CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-20. CBT-mixed interventions compared with relaxation: Head-to-head trials

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction by CAPS						
2; 85	Medium; RCTs	Consistent	Direct	Imprecise	WMD range -24.0 to -21.2, p<0.05 in 2 of 2 trials	Low
Disability/functional impairment by GHQ Global Improvement						
1; 45	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.15, p=NS	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-21. EMDR compared with inactive controls (waitlist, usual care)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction						
8; 449	Medium; RCTs	Consistent	Direct	Imprecise	SMD -1.08 (95% CI, -1.82 to -0.35)	Moderate
Loss of Diagnosis						
7; 427	Medium; RCTs	Consistent	Direct	Imprecise	RD 0.43 (0.25 to 0.61)	Moderate
Prevention/reduction of comorbid depression						
7; 347	Medium; RCTs	Consistent	Direct	Imprecise	SMD -0.91 (95% CI, -1.58 to -0.24)	Moderate
Prevention/reduction of comorbid anxiety: mean change from baseline in STAI						
4; 167	Medium; RCTs	Inconsistent	Direct	Imprecise	No significant difference in 3 of 4 trials.	Insufficient

CI = confidence interval; EMDR = eye movement desensitization and reprocessing; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial; RD = risk difference; SMD = Standardized mean difference; STAI = State Trait Anxiety Inventory; WMD = weighted mean difference

Table I-22. EMDR compared with relaxation

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction						
2; 64	Medium; RCTs	Inconsistent	Direct	Imprecise	Inconsistent findings across studies	Insufficient
Loss of Diagnosis at 3 month post-treatment followup						
2; 64	Medium; RCTs	Inconsistent	Direct	Imprecise	Inconsistent findings across studies	Insufficient
Prevention/reduction of comorbid depression: BDI						
2; 64	Medium; RCTs	Inconsistent	Direct	Imprecise	Inconsistent findings across studies	Insufficient
Prevention/reduction of comorbid anxiety: STAI						
1; 23	Medium; RCT	NA, single study	Direct	Imprecise	Cohen's d=1.15 (favoring EMDR), p<0.01	Insufficient

[a] Two SMDs reported here because two meta-analyses were run because one of the two trials reported two measures of PTSD symptoms.[46] The first SMD is from our meta-analysis using the Mississippi Scale for Combat Related PTSD from the study reporting two measures; the second is using the IES from that trial. The other trial reported the CAPS.[133]

BDI = Beck Depression Inventory; CAPS = Clinician-Administered Post Traumatic Stress Disorder Scale; CI = confidence interval; EMDR = eye movement desensitization and reprocessing; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-23. Seeking safety compared with inactive comparators

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS frequency and intensity, reduction from baseline to post-treatment						
3; 232	Medium; RCT	Consistent	Direct	Imprecise	SMD of indiv. trials ranged from -0,22 to 0.04; 2 of 33 trials failed trtmt (no study p<0.05)	Low for no difference
Prevention/reduction of comorbid substance use						
2; 163	Medium; RCT	Inconsistent	Direct	Imprecise	Mixed findings, p<0.05 for drug use but not alcohol use in 1 of 2 trials	Insufficient

CAPS = Clinician-Administered Post Traumatic Stress Disorder Scale; BDI = Beck Depression Inventory; CI = confidence interval; IES = Impact of Events Scale; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-24. Imagery rehearsal therapy (IRT) compared with waitlist (1 trial)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS mean change from baseline						
1; 168	Medium; RCT	NA, Single study	Direct	Imprecise	WMD -21.0, p<0.05	Low
Prevention/reduction of comorbid depression: HAMD						
1; 168	Medium; RCT	NA, Single study	Direct	Imprecise	p=ns	Insufficient
Prevention/reduction of comorbid anxiety: HAMA						
1; 168	Medium; RCT	NA, Single study	Direct	Imprecise	p=0.04 because symptoms increased in inactive comparator group at followup	Insufficient

CAPS = Clinician-Administered Post Traumatic Stress Disorder Scale; CI = confidence interval; HAM-D = Hamilton Depression Scale; HAM-A = Hamilton Anxiety Scale; IRT = imagery rehearsal therapy; NA = not applicable; NR = Not Reported; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial; SF-36 = 36-Item Short-Form Health Survey; WL = waitlist

Table I-25. Narrative exposure therapy (NET) compared with an inactive control (waitlist or MA)

	Domains Pertaining to Strength of evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline to post-treatment in PDS and CAPS						
3; 232	Medium; RCTs	Consistent	Direct	Imprecise	SMD ranged from -1.95 to -0.79 across 3 individual studies (3 of 3 studies p<0.05)	Moderate
Loss of Diagnosis						
2; 198	Medium; RCTs	Consistent	Direct	Imprecise	RD range 0.06 to 0.14, p<0.05 in 1 of 2 trials	Low
Prevention/reduction of comorbid depression						
2; 68	Medium; RCTs	Inconsistent	Direct	Imprecise	Mixed evidence	Insufficient
Prevention/reduction of comorbid pain						
1; 34	Medium; RCT	NA, single study	Direct	Imprecise	P<0.05	Insufficient

CI = confidence interval; HSCL-25 = Hopkins Symptom Check List-25; NA = not applicable; NR = not reported; PDS = Posttraumatic Stress Diagnostic Scale; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial; SOMS= Screening for Somatoform Symptoms Scale; SRQ-20 = Self-Reporting Questionnaire

Table I-26. Brief eclectic psychotherapy (BEP) compared with waitlist

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: various outcome measures						
1; 30 [a]	Medium; RCTs	NA, single study	Direct	Imprecise	WMD -10.8, p=ns	Insufficient
Symptom Remission						
1; 30	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.13, p=ns	Insufficient
Loss of Diagnosis						
3; 96	Medium; RCTs	Inconsistent	Direct	Imprecise	RD range 0.13 to 0.58 [b]	Low
Prevention/reduction of comorbid depression						
3; 96	Medium; RCTs	Inconsistent	Direct	Imprecise	P<0.05 in 3 of 3 studies	Low
Prevention/reduction of comorbid anxiety						
3; 96	Medium; RCTs	Inconsistent	Direct	Imprecise	P<0.05 in 3 of 3 studies	Low
Return to work						
2; 66	Medium; RCTs	Inconsistent	Direct	Imprecise	P<0.05 for 1 of 2 trials [c]	Insufficient

[a] The three trials used different outcome measures—two found small or medium effect sizes using the CAPS and SI-PTSD, respectively. The other did not report enough data to determine effect sizes.

[b] The three trials were consistent in the sense that they all found more subjects in the BEP group with loss of PTSD diagnosis compared with the WL group. However, the magnitude of the differences between groups was inconsistent

[c] One trials reported percentage of subjects on sick leave and the other reported percentage who had returned to work.

CI = confidence interval; mths = months; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-27. Brief eclectic psychotherapy (BEP) compared with EMDR

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: IES-R and SI-PTSD						
1; 140	Medium; RCT	NA, single study	Direct	Imprecise	p=ns	Insufficient
Loss of Diagnosis						
1; 140	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.08 favoring EMDR, p=ns	Insufficient
Prevention/reduction of comorbid depression: HADS depression						
1; 140	Medium; RCT	NA, single study	Direct	Imprecise	p=ns	Insufficient
Prevention/reduction of comorbid anxiety: HADS anxiety						
1; 140	Medium; RCT	NA, single study	Direct	Imprecise	p=ns	Insufficient

CI = confidence interval; mths, months; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-28. Trauma affect regulation compared with waitlist

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
2; 173	Medium; RCT	Consistent	Direct	Imprecise	Between-group mean difference of -17.4 and -2.7 in individual studies Both favored treatment (1 of 2 studies p<0.05)	low
Symptom Remission						
2; 173	Medium; RCT	Inconsistent	Direct	Imprecise	RD range -0.11 to 0.21, effect sizes in opposite directions	Insufficient
Loss of Diagnosis						
2; 173	Medium; RCT	Inconsistent	Direct	Imprecise	RD range 0.01 to 0.26	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 93	Medium; RCT	NA, single study	Direct	Imprecise	WMD -4.1, p<0.05	Insufficient
Prevention/reduction of comorbid anxiety						
1; 93	Medium; RCT	NA, single study	Direct	Imprecise	p=ns	Insufficient

BDI= Beck Depression Inventory; CI = confidence interval; mths, months; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-29. Interpersonal Therapy compared with Relaxation Therapy

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 72	Medium; RCT	NA, single study	Direct	Imprecise	WMD -6.3 favoring IPT, p<0.05	Insufficient
Remission (CAPS<20)						
1; 72	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.04 favoring IPT	Insufficient
Prevention/reduction of comorbid depression: HAM-D						
1; 72	Medium; RCT	NA, single study	Direct	Imprecise	WMD -0.3, p=ns	Insufficient
Quality of Life: Quality of Life Enjoyment and Satisfaction Questionnaire						
1; 72	Medium; RCT	NA, single study	Direct	Imprecise	WMD -10.1 favoring IPT, p<0.05	Insufficient
Function: Inventory of Interpersonal Problems Questionnaire						
1; 72	Medium; RCT	NA, single study	Direct	Imprecise	WMD -0.46 favoring IPT, p<0.05	Insufficient

CI = confidence interval; HAM-D= Hamilton Depression Rating Scale; NA = not applicable; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-30. Memory Specificity Training compared with control (no treatment)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: IES-R						
1; 24	Medium; RCT	NA, single study	Direct	Imprecise	Greater reduction in scores among MEST group vs. controls ($p<0.001$)[a]	Insufficient
Prevention/Reduction of Comorbid Depression: BDI-II						
1; 24	Medium; RCT	NA, single study	Direct	Imprecise	No difference between groups in score change from baseline (scores NR)	Insufficient

[a] Baseline and followup scores are shown in figure only.

BDI-II = Beck depression inventory II questionnaire; CI = confidence interval; IES-R =Impact of Event Scale- Revised; NA = not applicable; NS= not significant; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Table I-31. Structured Writing Therapy compared with usual care (substance abuse treatment)[a]

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: PDS						
1; 34	Medium; RCT	NA, single study	Direct	Imprecise	WMD -0.3	Insufficient
Symptom Remission						
1; 34	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.12, p=ns	Insufficient
Prevention/reduction of comorbid depression: reduction/remission of primary substance use diagnosis						
1; 34	Medium; RCT	NA, single study	Direct	Imprecise	Days abstinent WMD 2.1 Substance use disorder Remission: (34.1; p=NS	Insufficient

[a] Both groups received intensive treatment program for substance use disorders based on CBT and other components (e.g., individual therapy, social skills training, relapse prevention). No interventions related to PTSD symptoms were carried out during the usual substance abuse treatment program.

CI = confidence interval; NA = not applicable; NS= not significant; PDS = Posttraumatic Stress Diagnostic Scale; PTSD = post-traumatic stress disorder; RCT = randomized controlled trial

Key Question 2

Table I-32. Placebo-controlled trials of alpha-blockers (prazosin)

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design/ Quality**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
3; 117	Medium; RCTs	Consistent	Direct	Imprecise	SMD -0.52 (95% CI, -0.90 to -0.14)	Low
Prevention/reduction of comorbid depression						
1; 40	Medium; RCT	NA, single study	Direct	Imprecise	WMD -5.0, p=ns	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-33. Strength of evidence for divalproex compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
1; 85	Low; RCT	NA, single study	Direct	Imprecise	WMD -1.40, p=ns	Insufficient
Prevention/reduction of comorbid depression: MADRS						
1; 85	Low; RCT	NA, single study	Direct	Imprecise	WMD -0.6, p=ns	Insufficient
Prevention/reduction of comorbid anxiety: HAM-A						
1; 85	Low; RCT	NA, single study	Direct	Imprecise	WMD 1.4, p=ns	Insufficient

Table I-34. Strength of evidence for tiagabine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	Risk of Bias; Design	Consistency	Directness	Precision	Summary Effect Size (95% CI)	High, Moderate, Low, Insufficient
PTSD Symptom Reduction: CAPS						
1; 232	Medium; RCT	NA, single study	Direct	Imprecise	WMD -0.50, p-ns	Insufficient
Remission (CAPS less than 20)						
1; 232	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.02, p=ns	Insufficient
Disability/functional impairment: Sheehan Disability Scale						
1; 232	Medium; RCT	NA, single study	Direct	Imprecise	WMD 0.4, p=ns	Insufficient

Table I-35. Strength of evidence for topiramate compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	Risk of Bias; Design	Consistency	Directness	Precision	Summary Effect Size (95% CI)	High, Moderate, Low, Insufficient
PTSD Symptom Reduction: CAPS						
3; 142	Medium; RCT	Consistent	Direct	Imprecise	SMD ranged from -1.85 to -0.38 across individual studies	Low
Symptom Remission						
1; 40	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.21, p=ns	Insufficient
Prevention/reduction of comorbid depression: BDI or HAM-D						
2; 75	Medium; RCT	NA, single study	Direct	Imprecise	Both favored topiramate, p=ns in 2 of 2 trials	Insufficient
Prevention/reduction of comorbid anxiety: HAM-A						
1; 40	Medium; RCT	NA, single study	Direct	Imprecise	WMD -13.9, p=ns	Insufficient
Disability/functional impairment: Sheehan Disability Scale						
1; 40	Medium; RCT	NA, single study	Direct	Imprecise	WMD -4.8, p=ns	Insufficient

Table I-36. Olanzapine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design/ Quality**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS and SIPS						
CAPS 2; 47 All PTSD symptom scales 3; 62	Medium; RCT	Consistent	Direct	Imprecise	SMD (CAPS) of -1.15 and -0.96 across individual studies. Both significantly favored treatment SMD ranged from -1.15 to 0.89 across individual studies. All studies favored treatment (2 of 3 studies p<0.05)	Low
Prevention/reduction of comorbid depression: CES-D						
1; 19	Medium	NA, single study	Direct	Imprecise	WMD -0.37, p<0.05	Insufficient
Disability/functional impairment: Sheehan						
2; 43	Medium, RCT	Inconsistent	Direct	Imprecise	WMD range -4.2 to 0.3, 1 of 2 trials favored olanzapine, 1 of 2 trials favored placebo, p<0.05 for 1 of 2 trials	Insufficient
Return to work or return to active duty						
0; 0	NA	NA	NA	NA	NA	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial; SIPS = Single Item PTSD Screeners.

Table I-37. Risperidone compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design/ Quality**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS						
4; 422	Medium; RCTs	Inconsistent	Direct	Imprecise	SMD -0.26 (95% CI, -0.52 to -0.01) in 1 of 4 trials	Low
Prevention/reduction of comorbid depression: HAM-D						
1; 65	Medium; RCT	NA, single study	Direct	Imprecise	WMD -2.3, p=ns	Insufficient
Prevention/reduction of comorbid anxiety: HAM-A or PANSS						
2; 105	Medium; RCT	Consistent	Direct	Imprecise	p<0.05 for 2 of 2 trials, favoring risperidone	Low

CAPS = Clinician-Administered PTSD Scale; CI = confidence interval; HAM-A = Hamilton Anxiety Rating Scale; HAM-D = Hamilton Depression Rating Scale; NA = not applicable; PANSS = Positive and Negative Syndrome Scale; PTSD = posttraumatic stress disorder; RCT = randomized controlled trial; WMD = weighted mean difference.

Table I-38. Citalopram compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)[a]**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline in CAPS						
1; 35	Medium; RCT	NA, single study	Direct	Imprecise	WMD 8.0, favoring placebo, p=ns	Insufficient
Prevention/reduction of comorbid depression: BDI, mean change from baseline						
1; 35	Medium; RCT	NA, single study	Direct	Imprecise	WMD -0.47, p=ns	Insufficient

[a] Data are from a single trial comparing citalopram, sertraline, and placebo.[175]
CI = confidence interval; NA = not applicable; RCT = randomized controlled trial.

Table I-39. Fluoxetine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline in CAPS						
4 (5 comparisons); 835	Medium; RCTs	Consistent	Direct	Precise	SMD -0.28 (95% CI -0.42 to -0.14)	Moderate
Symptom Remission: Percent of subjects with CAPS less than 20						
1; 52	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.03, p=ns	Insufficient
Loss of Diagnosis: percent of subjects no longer meeting criteria for PTSD diagnosis						
1; 59	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.14, p=ns	Insufficient
Prevention/reduction of comorbid depression: mean change from baseline in MADRS						
3 (4 comparisons); 771	Medium; RCTs	Consistent	Direct	Precise	SMD -0.20 (95% CI -0.40 to 0.00)	Low for no difference
Prevention/reduction of comorbid anxiety: mean change from baseline in HAM-A						
2 (3 comparisons); 712	Medium; RCTs	Inconsistent	Direct	Imprecise	WMD range -3.0 to -1.5, both favored fluoxetine, p<0.05 in 1 of 2 trials	Low
Disability/functional impairment: mean change from baseline in SDS						
1; 54	Medium; RCT	NA, single study	Direct	Imprecise	WMD -5.8, p=ns	Insufficient

[a] Data from subgroup analysis of subjects with combat-related PTSD in one trial (N=144 of the 301 from the main trial).[173]

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-40. Paroxetine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline in CAPS						
2 (3 comparisons); 348	Medium; RCTs	Consistent	Direct	Imprecise	SMD of -0.56 to -0.44 in individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
Symptom Remission						
2; 348	Medium; RCTs	Consistent	Direct	Imprecise	RD of 0.13 and 0.19 across 2 individual studies (1 of 2 studies p<0.05)	Moderate
Prevention/reduction of comorbid depression: mean change from baseline in MADRS						
2 (3 comparisons); 348	Medium; RCTs	Consistent	Direct	Imprecise	SMD ranged from -0.60 to -0.34 across individual studies Both studies favored treatment (2 of 2 studies p<0.05)	Moderate
Disability/functional impairment: mean change from baseline in SDS						
2 (3 comparisons); 348	Medium; RCTs	Consistent	Direct	Imprecise	WMD range -2.6 to -1.9, both favored paroxetine, p<0.05 in 2 of 2 trials (3 of 3 comparisons)	Moderate

[a] Data are the best available evidence from a trial of paroxetine (N=323) that defined remission as a CAPS-2 total score less than 20 and found a significantly greater proportion of paroxetine-treated subjects achieved remission compared with placebo at week 12 (29.4% vs. 16.5%, p=0.008). The difference (12.9% difference between paroxetine and placebo) would translate to a number needed to treat of 7.8 to achieve one remission.[65] The other trial contributing data for this outcome found similar percentages of subjects achieving remission (33% vs. 14%), but it was underpowered to detect anything but a very large difference for this outcome.[174]

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-41. Sertraline compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: mean change from baseline in CAPS						
7; 1,085	Medium; RCTs	Consistent	Direct	Precise	SMD -0.20 (95% CI: -0.36 to -0.04)	Low
Symptom Remission: Percent of subjects achieving CAPS-SX_{17} score less than 20						
1; 352	Medium; RCT	NA, single study	Direct	Imprecise	RD 4.4, p=NS	Insufficient
Prevention/reduction of comorbid depression: mean change from baseline in HAM-D						
7; 1,085	Medium; RCTs	Inconsistent	Direct	Imprecise	SMD -0.14 (95% CI: -0.33 to 0.06)	Low for no difference
Prevention/reduction of comorbid anxiety: mean change from baseline in HAM-A						
2; 377	Medium; RCTs	Inconsistent	Direct	Imprecise	Effects in opposite direction, p=ns for 2 of 2 trials	Insufficient
Quality of Life: mean change in Q-LES-Q						
2; 539	Medium; RCTs	Consistent	Direct	Imprecise	WMD range -8.4 to -2.4, p<0.05 in 1 of 2 trials	Low
Disability/functional impairment: mean change from baseline in SDS						
1; 352	Medium; RCT	NA, single study	Direct	Imprecise	WMD -1.7, p=ns	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-42. Venlafaxine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design/ Quality**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: Change in CAPS						
2; 687	Medium/RCT	Consistent	Direct	Precise	SMD of -0.35 and -0.26 for two individual studies	Moderate
Symptom Remission: defined by CAPS-Sx total score of 20 or less						
2; 687	Medium/RCT	Consistent	Direct	Precise	RD of 0.12 and 0.15 across individual studies	Moderate
Prevention/reduction of comorbid depression: change in BDI						
2; 687	Medium/RCT	Consistent	Direct	Precise	Between-group mean difference of -2.6 and -1.6 across individual studies. Both studies favored treatment.	Moderate
Prevention/reduction of comorbid anxiety						
0; 0	NA	NA	NA	NA	NA	Insufficient
Quality of Life (change in Q-LES-Q-SF)						
2; 687	Medium/RCT	Consistent (I^2 0%)	Direct	Precise	WMD range 2.8 to 4.1, $p<0.05$ in 2 of 2 trials.	Moderate
Disability/functional impairment (change in SDS, and change in GAF)						
2; 687	Medium/RCT	Consistent (I^2 0%)	Direct	Precise	For SDS, WMD range -2.1 to -2.0, $p<0.05$ in 2 of 2 trials For GAF, WMD range 2.7 to 4.0, both trials favored venlafaxine, $p<0.05$ in 1 of 2 trials	Moderate

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-43. Placebo-controlled trials of bupropion

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Summary Effect Size (95% CI)	High, Moderate, Low, Insufficient
PTSD Symptom Reduction: CAPS						
1; 30	Medium; RCT	NA, Single Study	Direct	Imprecise	WMD 4.7, p=ns	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 30	Medium; RCT	NA, single study	Direct	Imprecise	0.4, p=ns	Insufficient

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-44. Placebo-controlled trials of mirtazapine

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	Risk of Bias; Design/ Quality	Consistency	Directness	Precision	Summary Effect Size (95% CI)	High, Moderate, Low, Insufficient
PTSD Symptom Reduction: DTS						
1; 29	Medium; RCT	NA, single study	Direct	Imprecise	WMD -9.5, p=ns	Insufficient
PTSD Symptom Reduction: SPRINT						
1; 29	Medium; RCT	NA, single study	Direct	Imprecise	WMD -3.76, p=ns	Insufficient
PTSD Symptom Reduction: SIPS						
1; 29	Medium; RCT	NA, single study	Direct	Imprecise	WMD -10.8, p<0.05	Insufficient
Prevention/reduction of comorbid depression: HADS-D						
1; 29	Medium; RCT	NA, single study	Direct	Imprecise	WMD -1.7, p=ns	Insufficient
Prevention/reduction of comorbid anxiety: HADS-A						
1; 29	Medium; RCT	NA, single study	Direct	Imprecise	WMD -1.6, p<0.05	Insufficient

Table I-45. Paroxetine + placebo compared with desipramine + placebo: Head-to-head trials[a]

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	Risk of Bias; Design	Consistency	Directness	Precision	Summary Effect Size (95% CI)	High, Moderate, Low, Insufficient
PTSD Symptom Reduction: CAPS, mean change from baseline						
1; 88	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -3.2 favoring desipramine+placebo, p<0.05	Low
Prevention/reduction of comorbid depression: HAM-D, mean change from baseline						
1; 88	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -1.3 favoring paroxetine+placebo, p=ns,	Low
Prevention/reduction of comorbid alcohol dependence: heavy drinking days and drinks per drinking day						
1; 88	Medium; RCT	NA, single study	Direct	Imprecise	Greater reduction with desipramine, p<0.05	Low

[a] Data are from 1 trial of veterans with PTSD and comorbid alcohol dependence that compared Paroxetine + Naltrexone, Paroxetine + Placebo, Desiprimine + Naltrexone, and Desipramine + Placebo.

[b] Data NR for drinking outcomes; p=0.009 for percentage of heavy drinking days and p=0.027 for drinks per drinking day; shown in Figure only; magnitude of difference NR and difficult to read clearly from the Figure, all groups ended up less than 20 standard drinks per week (from baselines above 70 drinks per week), but it appears that the Desipramine groups ended up in the 0 to 10 drinks per week range and the paroxetine groups ended up in the 10-20 range at the 12 week endpoint.

CI = confidence interval; NA = not applicable; NR = not reported; RCT = randomized controlled trial

Table I-46. Venlafaxine ER compared with sertraline: Head-to-head trials

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)[a]**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS-SX17, mean change from baseline						
1; 538	Medium; RCT	NA, single study[b]	Direct	Precise	WMD range, -2.1 favoring sertraline, p=ns	Low for no difference
Symptom Remission: SX17 score of ≤20 at week 12						
1; 538	Medium; RCT	NA, single study[b]	Direct	Precise	WMD, -5.9; p=ns,	Insufficient
Prevention/reduction of comorbid depression: HAM-D, mean change from baseline						
2; 745	Medium; RCT	Consistent	Direct	Imprecise	WMD range -0.7 to -0.1, p=ns in 2 of 2 trials	Moderate for no difference
Quality of Life: Q-LES-Q or WHO-5, mean change						
2; 745	Medium; RCT	Inconsistent	Direct	Imprecise	1 trial favored venlafaxine, the other favored sertraline, p=ns in both trials	Low for no difference
Disability/functional impairment: SDS						
2; 745	Medium; RCT	Inconsistent	Direct	Imprecise	1 trial favored venlafaxine, the other favored sertraline, p=ns in both trials	Low for no difference

[a] Data are from 1 multicenter trial comparing venlafaxine ER, sertraline, and placebo.[69]
[b] Although this is a single trial, it was a multicenter trial including 59 outpatient centers in the US. We considered this in our SOE grade.

CI = confidence interval; NA = not applicable; NR = not reported; p=placebo; RCT = randomized controlled trial; S = sertraline; V = venlafaxine ER

Table I-47. Sertraline compared with citalopram: Head-to-head trials

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)[a]**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS, mean change from baseline						
1; 58	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -11.1 favoring sertraline, p=ns	Insufficient
PTSD Symptom Reduction: IES, mean change from baseline						
1; 58	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -5.9; p=ns,	Insufficient
Prevention/reduction of comorbid depression: BDI						
1; 58	Medium; RCT	NA, single study	Direct	Imprecise	WMD, -2.9; p=ns	Insufficient

[a] Data are from 1 RCT comparing sertraline, citalopram, and placebo.[175]

C = citalopram; CI = confidence interval; NA = not applicable; NR = not reported; p=placebo; RCT = randomized controlled trial; S = sertraline

Key Question 3

Table I-48. Head-to-head trials of psychological and pharmacological treatments: Fluoxetine compared with EMDR

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Mean, %, or Effect Size (ES)**	**High, Moderate, Low, Insufficient**
PTSD Symptom Reduction: CAPS and PSS						***Insufficient***
Fluoxetine vs. EMDR 1; 59	Medium; RCT	Unknown (single study)	Direct	Imprecise	WMD -10.1 favoring fluoxetine, p=ns	Insufficient
Symptom Remission:						
Fluoxetine vs. EMDR 1; 59	Medium; RCT	Unknown (single study)	Direct	Imprecise	RD 0.15, p=ns	Insufficient
Loss of Diagnosis						
Fluoxetine vs. EMDR 1; 59 (post) 1; 50 (f/up)	Medium; RCT	Unknown (single study)	Direct	Imprecise	RD 0.03 favoring EMDR, p=ns	Insufficient
Prevention/reduction of comorbid depression						
Fluoxetine vs. EMDR 1; 59 (post 1; 50 (f/up)	Medium; RCT	Unknown (single study)	Direct	Imprecise	WMD -1.9, p=ns favoring EMDR	Insufficient

BDI = Beck Depression Inventory; CAPS = Clinician-Administered PTSD Scale – total; f/up, 6 month followup; NR = not reported; NS = non-significant; post = post-treatment; wk = week.

Key Question 4

Table I-49. Strength of evidence for adverse events for fluoxetine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
Withdrawals due to Adverse Events						
3; 712	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial showed no difference, one trial favored fluoxetine, and one had two arms providing conflicting results; p=ns in 3 of 3 trials	Insufficient
Headaches						
3; 776	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial favored fluoxetine, two favored placebo; p=ns in 3 of 3 trials	Insufficient
Nausea						
2; 712	Medium; RCTs	Consistent	Direct	Imprecise	Range 0.03 to 0.07 across two trials; p=ns in both trials	Low
Insomnia						
1; 301	Medium; RCT	NA, single study	Direct	Imprecise	One study favored placebo, p=ns	Insufficient
Diarrhea						
1; 44	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.24, p<0.05	Low
Somnolence						
1; 411	Medium; RCT	NA, single study	Direct	Imprecise	RD range 0.04 to 0.06 (variation by dose), p-ns	Low

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-50. Strength of evidence for adverse events for paroxetine compared with placebo

	Domains Pertaining to Strength of evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
Withdrawals due to Adverse Events						
3; 911	Medium; RCTs	Consistent	Direct	Imprecise	All three studies favored placebo, p=ns in 3 of 3 studies	Insufficient
Nausea						
1; 323	Medium; RCTs	NA, single study	Direct	Imprecise	RD 0.11, p<0.05[a]	Low
Dry mouth						
1; 323	Medium; RCT	NA, single study	Direct	Imprecise	RD 0.10, p<0.05	Low
Diarrhea						
1; 563	Medium; RCT	NA, single study	Direct	Imprecise	Incidence of at least 10% and twice that of placebo[64]	Insufficient
Somnolence						
1; 323	Medium; RCTs	Consistent	Direct	Imprecise	RD 0.13, p<0.05[a]	Low
Drowsiness						
1; 25	Medium; RCT	NA, single study	Direct	Imprecise	One study favored paroxetine, p=ns	Insufficient
Sexual adverse effects						
1; 563	Medium; RCT	NA, single study	Direct	Imprecise	Incidence of at least 10% and twice that of placebo[64]	Insufficient

[a] Data are based on the only trial (N=323) reporting sufficient data to determine the risk difference.[65] One additional trial (N=563) that provided narrative description reported that the most commonly reported adverse events associated with paroxetine use (with an incidence of at least 10% and twice that of placebo) were asthenia, diarrhea, abnormal ejaculation, impotence, nausea, and somnolence.[64]

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Table I-51. Strength of evidence for adverse events for venlafaxine compared with placebo

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Number of Studies; Number of Subjects	**Risk of Bias; Design**	**Consistency**	**Directness**	**Precision**	**Summary Effect Size (95% CI)**	**High, Moderate, Low, Insufficient**
Withdrawals due to Adverse Events						
2; 687	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial favored venlafaxine, one trial favored placebo; none were statistically significant	Insufficient
Headaches						
2; 687	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial favored venlafaxine, one trial favored placebo; none were statistically significant	Insufficient
Nausea						
2; 686	Medium; RCTs	Consistent	Direct	Precise	Both trials favored placebo to a statistically significant degree	Moderate
Insomnia						
2; 687	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial favored venlafaxine, one trial favored placebo; none were statistically significant	Insufficient
Dry mouth						
2; 687	Medium; RCTs	Consistent	Direct	Imprecise	RD range 0.04 to 0.08, p<0.05 in 1 of 2 trials	Low
Diarrhea						
1; 358	Medium; RCTs	NA, single study	Direct	Imprecise	P=ns	Insufficient
Dizziness						
2; 687	Medium; RCTs	Inconsistent	Direct	Imprecise	P=ns	Insufficient
Fatigue						
2; 687	Medium; RCTs	Inconsistent	Direct	Imprecise	Both trials favored placebo, none to a statistically significant degree	Insufficient
Somnolence						
2; 687	Medium; RCTs	Inconsistent	Direct	Imprecise	One trial favored venlafaxine, one trial favored placebo; none were statistically significant	Insufficient
Decreased appetite						
1; 358	Medium; RCTs	NA, single study	Direct	Imprecise	One trial favored venlafaxine, but not to a statistically significant degree	Insufficient

	Domains Pertaining to Strength of Evidence				Magnitude of Effect	Strength of Evidence
Constipation						
2; 686	Medium; RCTs	Consistent	Direct	Imprecise	RD range 0.02 to 0.09 across 2 trials, p<0.05 in 1 of 2 trials	Low

CI = confidence interval; NA = not applicable; RCT = randomized controlled trial

Appendix J. Expert Guidance and Review

Stakeholder Input in Formulating the Research Protocol

Stakeholders, including Key Informants and Technical Experts, participated in a virtual workshop by PCORI in December 2016 to help formulate the research protocol. Details on the virtual workshop, including a list of participants, can be found at https://www.pcori.org/events/2016/updating-systematic-reviews-pcori-virtual-multi-stakeholder-workshop-psychological-and.

Key Informants in the workshop included end users of research, such as patients and caregivers, practicing clinicians, relevant professional and consumer organizations, purchasers of health care, and others with experience in making health care decisions. Technical Experts in the workshop included multidisciplinary groups of clinical, content, and methodological experts who provided input in defining populations, interventions, comparisons, and outcomes, and identified particular studies or databases to search. They were selected to provide broad expertise and perspectives specific to posttraumatic stress disorder (PTSD).

During the virtual workshop, stakeholders reviewed scoping for the updated review, prioritized key questions, and discussed where the evidence base has accumulated since the prior review, as well as emerging issues in PTSD. Based upon findings from the workshop, the PTSD protocol was developed by the EPC with guidance from PCORI and AHRQ.

Key Informants and Technical Experts did not do analysis of any kind or contribute to the writing of this draft report. They will be given the opportunity to review the report through the peer or public review mechanisms.

Peer Reviewers

Prior to publication of the final evidence report, EPCs sought input from independent Peer Reviewers without financial conflicts of interest. However, the conclusions and synthesis of the scientific literature presented in this report does not necessarily represent the views of individual reviewers.

Peer Reviewers must disclose any financial conflicts of interest greater than $10,000 and any other relevant business or professional conflicts of interest. Because of their unique clinical or content expertise, individuals with potential non-financial conflicts may be retained. The TOO and the EPC work to balance, manage, or mitigate any potential non-financial conflicts of interest identified.

The list of Peer Reviewers follows:

Lieutenant Patrick M. High, Dr.P.H.
Substance Abuse and Mental Health Services Administration
Rockville, MD

Helena Kraemer, Ph.D.
Emeritus Faculty, Psychiatry and Behavioral Sciences
Stanford University
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Terri Pigott, Ph.D.
Associate Provost for Research and Professor of Research Methodology, School of Education
Loyola University Chicago
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Paula P. Schnurr, Ph.D.
Executive Director, National Center for PTSD
White River Junction, VT

Jeffrey Sonis, M.D., M.P.H.
Associate Professor of Social Medicine and Associate Professor of Family Medicine
University of North Carolina at Chapel Hill
Chapel Hill, NC

Appendix K. PCORI Checklist

PCORI Methodology Standards Checklist: SER Update					
Contract No.					
Task Order No.					
EPC					
Project Title	Psychological and Pharmacological Treatments for Adults with Posttraumatic Stress Disorder (PTSD): A Systematic Review Update				
Standard Category	Abbrev.	Standard	Is this standard appli-cable to this SER update?	List sections and pages of the SER report where you address this standard	If applicable, describe how and why the SER update deviated from this standard?
Cross-Cutting Standards					
Standards for Formulating Research Questions	RQ-1	Identify Gaps in Evidence	Yes	Introduction (pgs. 5-6)	
	RQ-2	Develop a Formal Study Protocol	Yes	Pre-report protocol	
	RQ-3	Identify Specific Populations and Health Decision(s) Affected by the Research	Yes	Methods (pgs. 9-10)	

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Standards for Formulating Research Questions (continued)	RQ-4	Identify and Assess Participant Subgroups	Yes	Introduction: KQ 1a, 2a, 3a (pg. 6) Methods: PICOTS (Table 2, pgs. 9-10)	
	RQ-5	Select Appropriate Interventions and Comparators	Yes	Methods: PICOTS (Table 2, pgs. 9-10)	
	RQ-6	Measure Outcomes that People Representing the Population of Interest Notice and Care About	Yes	Methods: PICOTS (Table 2, pgs. 9-10)	

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Standards Associated with Patient-Centered-ness	PC-1	Engage People Representing the Population of Interest and Other Relevant Stakeholders in Ways that are Appropriate and Necessary in a Given Research Context.	Yes	Participated in stakeholder call and will review draft report	
	PC-2	Identify, Select, Recruit, and Retain Study Participants Representative of the Spectrum of the Population of Interest and Ensure that Data Are Collected Thoroughly and Systematically from All Study Participants	N/A		Systematic review with no primary data collection

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Standards Associated with Patient-Centered-ness (continued)	PC-3	Use Patient-Reported Outcomes When Patients or People at Risk of a Condition Are the Best Source of Information	N/A		Systematic review with no primary data collection
	PC-4	Support Dissemination and Implementation of Study Results	N/A		Intent is to publish report and possibly a journal article with findings from the review when completed
Standards for Data Integrity and Rigorous Analyses	IR-1	Assess Data Source Adequacy	Yes	Methods (pgs. 8-13)	

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Standards for Data Integrity and Rigorous Analyses (continued)	IR-2	Describe Data Linkage Plans, if Applicable	N/A		N/A no data linkage required
	IR-3	A priori, Specify Plans for Data Analysis that Correspond to Major Aims	Yes	Methods (pgs. 12-13)	
	IR-4	Document Validated Scales and Tests	Yes	Results: Table 4 (pg. 17), Appendix	
	IR-5	Use Sensitivity Analyses to Determine the Impact of Key Assumptions	Yes	Appendix	

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Standards for Data Integrity and Rigorous Analyses (continued)	IR-6	Provide Sufficient Information in Reports to Allow for Assessments of the Study's Internal and External Validity	Yes	Evidence Tables in Appendix , Applicability section of Discussion (pgs. 113-114)	
Standards for Preventing and Handling Missing Data	MD-1	Describe in Protocol Methods to Prevent and Monitor Missing Data	Yes	Pre-report protocol documentation of assessment of publication bias and reporting bias	

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Standards for Preventing and Handling Missing Data (continued)	MD-2	Describe Statistical Methods to Handle Missing Data in Protocol	Yes	Pre-report protocol documentation of assessment of publication bias and reporting bias	
	MD-3	Use Validated Methods to Deal with Missing Data that Properly Account for Statistical Uncertainty Due to Missingness	N/A		Standard does not apply
	MD-4	Record and Report All Reasons for Dropout and Missing Data, and Account for All Patients in Reports	N/A		Standard does not apply

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Standards for Preventing and Handling Missing Data (continued)	MD-5	Examine Sensitivity of Inferences to Missing Data Methods and Assumptions, and Incorporate into Interpretation	N/A		Standard does not apply
Standards for Heterogeneity of Treatment Effect (HTE)	HT-1	State the Goals of HTE Analyses	Yes	Methods (pgs. 12-13)	
	HT-2	For all HTE Analyses, Pre-specify the Analysis Plan; for Hypothesis-Driven HTE Analyses, Pre-specify Hypotheses and Supporting Evidence Base	Yes	Methods (pgs. 12-13)	

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Standards for Heterogeneity of Treatment Effect (HTE) (continued)	HT-3	All HTE Claims Must be based on Appropriate Statistical Contrasts among Groups Being Compared, such as Interaction Tests or Estimates of Differences in Treatment Effect	Yes	Methods (pgs. 12-13)	
	HT-4	For any HTE Analysis, Report All Pre-specified Analyses and, at Minimum, the Number of Post hoc Analyses, Including all Subgroups and Outcomes Analyzed	Yes	Results: KQ 1a (pgs. 70-72), 2a (pgs. 95-98), 3a (pgs. 100-101)	
Standards for Specific Study Designs and Methods					
Standards for Data Registries	DR-1	Requirements for the Design and Features of Registries	N/A		Standard does not apply

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Standards for Data Registries (continued)	DR-2	Standards for Selection and Use of Registries	N/A		Standard does not apply
	DR-3	Robust Analysis of Confounding Factors	N/A		Standard does not apply
Standards for Data Networks as Research-Facilitating Structures	DN-1	Requirements for the Design and Features of Data Networks	N/A		Standard does not apply
	DN-2	Standards for Selection and Use of Data Networks	N/A		Standard does not apply
Causal Inference Standards	CI-1	Define Analysis Population Using Covariate Histories	N/A		Standard does not apply

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Causal Inference Standards (continued)	CI-2	Describe Population that Gave Rise to the Effect Estimate(s)	N/A		Standard does not apply
	CI-3	Precisely Define the Timing of the Outcome Assessment Relative to the Initiation and Duration of Exposure	N/A		Standard does not apply
	CI-4	Measure Confounders before Start of Exposure. Report Data on Confounders with Study Results	N/A		Standard does not apply

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Causal Inference Standards (continued)	CI-5	Report the Assumptions Underlying the Construction of Propensity Scores and the Comparability of the Resulting Groups in Terms of the Balance of Covariates and Overlap	N/A		Standard does not apply
	CI-6	Assess the Validity of the Instrumental Variable (i.e. How the Assumption are Met) and Report the Balance of Covariates in the Groups created by the IV for all IV analyses	N/A		Standard does not apply

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Standards for Adaptive and Bayesian Trial Designs	AT-1	Specify Planned Adaptations and Primary Analysis	N/A		Standard does not apply
	AT-2	Evaluate Statistical Properties of Adaptive Design	N/A		Standard does not apply
	AT-3	Specify Structure and Analysis Plan for Bayesian Adaptive Randomized Clinical Trial Designs	N/A		Standard does not apply
	AT-4	Ensure Clinical Trial Infrastructure Is Adequate to Support Planned Adaptation(s)	N/A		Standard does not apply

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	AT-5	Use the CONSORT statement, with Modifications, to Report Adaptive Randomized Clinical Trials	N/A		Standard does not apply
Standards for Studies of Diagnostic Tests	DT-1	Specify Clinical Context and Key Elements of Diagnostic Test Study Design	N/A		Standard does not apply
	DT-2	Study Design Should be Informed by Investigations of the Clinical Context of Testing	N/A		Standard does not apply
	DT-3	Assess the Effect of Factors Known to Affect Diagnostic Performance and Outcomes	N/A		Standard does not apply
	DT-4	Structured Reporting of Diagnostic Comparative Effectiveness Study Results	N/A		Standard does not apply

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Standards for Studies of Diagnostic Tests (continued)	DT-5	Focus Studies of Diagnostic Tests on Patient Centered Outcomes, Using Rigorous Study Designs with Preference for Randomized Controlled Trials	N/A		Standard does not apply
Standards for Systematic Reviews	SR-1	Adopt the Institute of Medicine (IOM) Standards for Systematic Reviews of Comparative Effectiveness Research, with Some Qualifications	Yes	Entire report (all pages)	

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